******* INVENTOR RESULTS *******

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=> d his l34

     (FILE 'HCAPLUS' ENTERED AT 09:44:39 ON 19 JUL 2007)
L34            5 S L33 NOT L1

=> d que l34
L1             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  US20060240095/PN
L30          187 SEA FILE=HCAPLUS ABB=ON  PLU=ON  JUNIEN J?/AU
L31           95 SEA FILE=HCAPLUS ABB=ON  PLU=ON  JUNIEN JEAN LOUIS/AU
L32          295 SEA FILE=HCAPLUS ABB=ON  PLU=ON  EDGAR A?/AU
L33            6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L32 AND ((L30 OR L31))
L34            5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L33 NOT L1


=> d hisl145
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU, BIOTECHNO,
PASCAL' - CONTINUE? (Y)/N:n


=> d his l45

     (FILE 'WPIX' ENTERED AT 09:51:45 ON 19 JUL 2007)
L45            6 S L43 NOT L1

=> d que l45
L1             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  US20060240095/PN
L30          187 SEA FILE=HCAPLUS ABB=ON  PLU=ON  JUNIEN J?/AU
L31           95 SEA FILE=HCAPLUS ABB=ON  PLU=ON  JUNIEN JEAN LOUIS/AU
L41           35 SEA FILE=WPIX ABB=ON  PLU=ON  (L30 OR L31)
L42          105 SEA FILE=WPIX ABB=ON  PLU=ON  EDGAR A?/AU
L43            7 SEA FILE=WPIX ABB=ON  PLU=ON  L41 AND L42
L45            6 SEA FILE=WPIX ABB=ON  PLU=ON  L43 NOT L1


=> d his l60

     (FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU, BIOTECHNO, PASCAL, CONFSCI'
     ENTERED AT 09:56:47 ON 19 JUL 2007)
L60           17 S L59 AND L24
                SAVE L60 TEMP KUD523MULTIN/A

     FILE 'STNGUIDE' ENTERED AT 10:25:38 ON 19 JUL 2007

=> d que l60
L15               QUE  ABB=ON  PLU=ON  STATIN
L16               QUE  ABB=ON  PLU=ON  METFORMIN
L17               QUE  ABB=ON  PLU=ON  HYPERGLYCEMI? OR DIABETE# METILLUS
L18               QUE  ABB=ON  PLU=ON  HYPERGLYCEMI? (2A) AGENT#
L19               QUE  ABB=ON  PLU=ON  DIABET? (2A) (TYPE 2 OR TYPE II OR T
                  YPE TWO)
L24               QUE  ABB=ON  PLU=ON  AY<2003 OR PY<2003 OR PRY<2003 OR MY
                  <2003 OR REVIEW/DT
L30          187 SEA FILE=HCAPLUS ABB=ON  PLU=ON  JUNIEN J?/AU
L31           95 SEA FILE=HCAPLUS ABB=ON  PLU=ON  JUNIEN JEAN LOUIS/AU
L32          295 SEA FILE=HCAPLUS ABB=ON  PLU=ON  EDGAR A?/AU
L35           45 SEA FILE=WPIX ABB=ON  PLU=ON  L15 AND L16
L36         6049 SEA FILE=WPIX ABB=ON  PLU=ON  (L17 OR L18 OR L19)
L41           35 SEA FILE=WPIX ABB=ON  PLU=ON  (L30 OR L31)
L55          719 SEA L41
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L56          474 SEA L32
L57           12 SEA L55 AND ((L35 OR L36))
L58            5 SEA L56 AND ((L35 OR L36))
L59           17 SEA L57 OR L58
L60           17 SEA L59 AND L24


=> dup rem l34 l45 l60
FILE 'HCAPLUS' ENTERED AT 10:29:00 ON 19 JUL 2007
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FILE 'PASCAL' ENTERED AT 10:29:00 ON 19 JUL 2007
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PROCESSING COMPLETED FOR L34
PROCESSING COMPLETED FOR L45
PROCESSING COMPLETED FOR L60
L61           12 DUP REM L34 L45 L60 (16 DUPLICATES REMOVED)
                 ANSWERS '1-5' FROM FILE HCAPLUS
                 ANSWER '6' FROM FILE WPIX
                 ANSWERS '7-9' FROM FILE MEDLINE
                 ANSWERS '10-12' FROM FILE BIOSIS

=> d 1-12 ibib ab 1-12

L61  ANSWER 1 OF 12  HCAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2006:91402  HCAPLUS  Full-text
DOCUMENT NUMBER:          144:156789
TITLE:                    Pharmaceutical combinations containing an inhibitor of
                          platelet aggregation and a fibrate
INVENTOR(S):              Edgar, Alan; Junien, Jean-Louis;
                          Wilkins, Michael
PATENT ASSIGNEE(S):       Fournier Laboratories Ireland Limited, Ire.
SOURCE:                   Eur. Pat. Appl., 14 pp.
                          CODEN: EPXXDW
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1621200	A1	20060201	EP 2004-291896	20040726
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
AU 2005266310	A1	20060202	AU 2005-266310	20050725
CA 2574920	A1	20060202	CA 2005-2574920	20050725
WO 2006010748	A1	20060202	WO 2005-EP53603	20050725
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
EP 1778247	A1	20070502	EP 2005-769894	20050725
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU				
CN 1988910	A	20070627	CN 2005-80025353	20050725
PRIORITY APPLN. INFO.:			EP 2004-291896 A	20040726
			WO 2005-EP53603 W	20050725

AB The present invention relates to a novel pharmaceutical combination, containing an inhibitor of platelet aggregation and a fibrate, where the inhibitor of platelet aggregation is preferably either aspirin or clopidogrel. Such a pharmaceutical combination of an inhibitor of platelet aggregation and a fibrate is expected to be useful in the treatment and/or prevention of myocardial infarction (heart attack), cardiac arrest, peripheral vascular disease (including symptomatic carotid artery disease), congestive heart failure, ischemic heart disease, angina pectoris (including unstable angina), sudden cardiac death, unstable angina, as well as cerebrovascular events such as cerebral infarction, cerebral thrombosis, cerebral ischemia and transient ischemic attack, disorders related to bypass operations (angioplasty), fitting of endovascular prostheses and restenosis, and inflammatory disorders, including arthritic conditions such as rheumatoid arthritis and osteoarthritis, as well as asthma or related airway or respiratory inflammatory disorders.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2005:1075612 HCAPLUS Full-text
DOCUMENT NUMBER: 143:339595
TITLE: Use of metformin and orlistat for the treatment or prevention of obesity
INVENTOR(S): Junien, Jean-Louis; Edgar, Alan
PATENT ASSIGNEE(S): Fournier Laboratories Ireland Limited, Ire.
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005092311	A1	20051006	WO 2005-EP2642	20050311
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1591114	A1	20051102	EP 2004-300137	20040312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
AU 2005226847	A1	20051006	AU 2005-226847	20050311
CA 2559461	A1	20051006	CA 2005-2559461	20050311
EP 1722770	A1	20061122	EP 2005-715996	20050311
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
CN 1929832	A	20070314	CN 2005-80007925	20050311
US 2007060532	A1	20070315	US 2006-518988	20060912
NO 2006004124	A	20060926	NO 2006-4124	20060913
PRIORITY APPLN. INFO.:			EP 2004-300137 A	20040312
			WO 2005-EP2642 W	20050311

AB The invention relates to the use of metformin and orlistat to treat patients suffering from obesity. Combination metformin and orlistat administration controlled body weight significantly better in mice fed high-fat diets compared to treatment with metformin or orlistat alone.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2004:753137 HCAPLUS Full-text
DOCUMENT NUMBER: 141:254589
TITLE: Combined use of a fibrate and orlistat for the treatment of obesity
INVENTOR(S): Junien, Jean-Louis; Edgar, Alan
PATENT ASSIGNEE(S): Fournier Laboratories Ireland Limited, Ire.
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1457206	A1	20040915	EP 2003-290625	20030313
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
AU 2004218938	A1	20040923	AU 2004-218938	20040312
CA 2518205	A1	20040923	CA 2004-2518205	20040312
WO 2004080450	A2	20040923	WO 2004-EP4010	20040312
WO 2004080450	A3	20050224		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG

EP 1601352	A2	20051207	EP 2004-720007	20040312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
BR 2004008322	A	20060314	BR 2004-8322	20040312
CN 1826108	A	20060830	CN 2004-80006891	20040312
JP 2006520365	T	20060907	JP 2006-505148	20040312
NO 2005004700	A	20051012	NO 2005-4700	20051012
US 2007078179	A1	20070405	US 2006-548909	20060913
PRIORITY APPLN. INFO.:			EP 2003-290625 A	20030313
			WO 2004-EP4010 A	20040312

AB The invention discloses the use of a fibrate and orlistat to treat patients suffering from obesity.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2004:446887 HCAPLUS Full-text
DOCUMENT NUMBER: 140:417962
TITLE: Combination of a ppar alpha agonist and metformin for treatment of metabolic syndrome including obesity by decreasing the serum triglycerides
INVENTOR(S): Junien, Jean-Louis; Edgar, Alan; Chaput, Evelyne
PATENT ASSIGNEE(S): Fournier Laboratories Ireland Limited, Ire.
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1424070	A1	20040602	EP 2002-292940	20021128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CA 2507894	A1	20040610	CA 2003-2507894	20031126
WO 2004047831	A2	20040610	WO 2003-EP13302	20031126
WO 2004047831	A3	20050224		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003288175	A1	20040618	AU 2003-288175	20031126
EP 1569634	A2	20050907	EP 2003-780062	20031126

EP 1569634	B1	20070516			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003016810	A	20051018	BR 2003-16810		20031126
JP 2006508995	T	20060316	JP 2004-554485		20031126
CN 1777417	A	20060524	CN 2003-80104445		20031126
AT 362362	T	20070615	AT 2003-780062		20031126
NO 2005002549	A	20050610	NO 2005-2549		20050526
MX 2005PA05707	A	20050726	MX 2005-PA5707		20050527
US 2006142397	A1	20060629	US 2005-536660		20050915
PRIORITY APPLN. INFO.:			EP 2002-292940	A	20021128
			WO 2003-EP13302	W	20031126

AB The present invention discloses methods of the combined use of a PPARα agonist, metformin and a pharmaceutically acceptable carrier for decreasing serum triglycerides, the treatment of metabolic syndrome including obesity. PPAR alpha agonists are a fibrate selected from the group consisting of gemfibrozil, fenofibrate, bezafibrate, clofibrate, ciprofibrate.

L61 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2004:117217 HCAPLUS Full-text
DOCUMENT NUMBER: 140:157488
TITLE: Use of fibrate to treat weight gain associated with rosiglitazone treatment
INVENTOR(S): Junien, Jean Louis; Edgar, Alan; Chaput, Evelyne
PATENT ASSIGNEE(S): Laboratoires Fournier S.A., Fr.
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1388351	A1	20040211	EP 2002-291994	20020808
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
EP 1388352	A1	20040211	EP 2002-292830	20021114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CA 2493747	A1	20040304	CA 2003-2493747	20030806
WO 2004018041	A1	20040304	WO 2003-EP8756	20030806
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003260380	A1	20040311	AU 2003-260380	20030806
EP 1526894	A1	20050504	EP 2003-792272	20030806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1674959	A	20050928	CN 2003-819135	20030806
JP 2005539033	T	20051222	JP 2004-530101	20030806

US 2004110799	A1	20040610	US 2003-636670	20030808
NO 2005000526	A	20050302	NO 2005-526	20050131
PRIORITY APPLN. INFO.:			EP 2002-291994 A	20020808
			EP 2002-292830 A	20021114
			WO 2003-EP8756 W	20030806

AB The present invention relates to the use of a fibrate to treat patients suffering from weight gain associated with rosiglitazone treatment.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 6 OF 12 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-181908 [18] WPIX
CROSS REFERENCE: 2004-171033
DOC. NO. CPI: C2004-072058 [18]
TITLE: Use of peroxisome proliferator-activated receptor-alpha agonist for treating weight gain associated with peroxisome proliferator-activated receptor-gamma agonist treatment
DERWENT CLASS: B05
INVENTOR: CHAPUT E; EDGAR A; EDGAR A D; JUNIEN J; JUNIEN J L
PATENT ASSIGNEE: (CHAP-I) CHAPUT E; (EDGA-I) EDGAR A; (JUNI-I) JUNIEN J; (LFOU-C) LAB FOURNIER SA
COUNTRY COUNT: 104

PATENT INFO ABBR.:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
EP 1388352	A1	20040211	(200418)*	EN	10[0]	
WO 2004018041	A1	20040304	(200418)	EN		
US 20040110799	A1	20040610	(200438)	EN		
AU 2003260380	A1	20040311	(200457)	EN		
EP 1526894	A1	20050504	(200530)	EN		
NO 2005000526	A	20050302	(200530)	NO		
JP 2005539033	W	20051222	(200604)	JA	24	
CN 1674959	A	20050928	(200610)	ZH		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1388352	A1	EP 2002-292830	20021114
AU 2003260380	A1	AU 2003-260380	20030806
EP 1526894	A1	EP 2003-792272	20030806
WO 2004018041	A1	WO 2003-EP8756	20030806
EP 1526894	A1	WO 2003-EP8756	20030806
NO 2005000526	A	WO 2003-EP8756	20030806
JP 2005539033	W	WO 2003-EP8756	20030806
US 20040110799	A1	US 2003-636670	20030808
JP 2005539033	W	JP 2004-530101	20030806
NO 2005000526	A	NO 2005-526	20050131
CN 1674959	A	CN 2003-819135	20030806

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2003260380 A1	Based on	WO 2004018041 A
EP 1526894 A1	Based on	WO 2004018041 A

JP 2005539033 W Based on WO 2004018041 A

PRIORITY APPLN. INFO: EP 2002-291994 20020808
EP 2002-292830 20021114

AB EP 1388352 A1 UPAB: 20060121
NOVELTY - Weight gain associated with a peroxisome proliferator-activated receptor (PPAR)-gamma agonist treatment is reduced by co-administering PPAR-alpha agonist and a PPAR-gamma agonist.
ACTIVITY - Anorectic. Male homozygous Zucker rats were per orally administered with a combination of fenofibrate (100 mg/kg) and rosiglitazone (0.3 mg/kg) twice daily. The results showed a reduction in body weight gain on co-administration of fenofibrate with rosiglitazone.
MECHANISM OF ACTION - PPAR-Agonist-Alpha; PPAR-Agonist-Gamma.
USE - In the manufacture of a medicament for decreasing the body weight gain associated with PPAR-gamma agonist treatment (claimed).

L61 ANSWER 7 OF 12 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2002240527 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11978643
TITLE: Chronic inhibition of circulating dipeptidyl peptidase IV by FE 999011 delays the occurrence of diabetes in male zucker diabetic fatty rats.
AUTHOR: Sudre Beatrice; Broqua Pierre; White Richard B; Ashworth Doreen; Evans D Michael; Haigh Robert; Junien Jean-Louis; Aubert Michel L
CORPORATE SOURCE: Ferring Research Institute and Division of Biology of Growth and Reproduction, Department of Pediatrics, University of Geneva School of Medicine, Geneva, Switzerland.
SOURCE: Diabetes, (2002 May) Vol. 51, No. 5, pp. 1461-9.
Journal code: 0372763. ISSN: 0012-1797.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 30 Apr 2002
Last Updated on STN: 28 May 2002
Entered Medline: 23 May 2002

AB Acute suppression of dipeptidyl peptidase IV (DPP-IV) activity improves glucose tolerance in the Zucker fatty rat, a rodent model of impaired glucose tolerance, through stabilization of glucagon-like peptide (GLP)-1. This study describes the effects of a new and potent DPP-IV inhibitor, FE 999011, which is able to suppress plasma DPP-IV activity for 12 h after a single oral administration. In the Zucker fatty rat, FE 999011 dose-dependently attenuated glucose excursion during an oral glucose tolerance test and increased GLP-1 (7-36) release in response to intraduodenal glucose. Chronic treatment with FE 999011 (10 mg/kg, twice a day for 7 days) improved glucose tolerance, as suggested by a decrease in the insulin-to-glucose ratio. In the Zucker diabetic fatty (ZDF) rat, a rodent model of type 2 diabetes, chronic treatment with FE 999011 (10 mg/kg per os, once or twice a day) postponed the development of diabetes, with the twice-a-day treatment delaying the onset of hyperglycemia by 21 days. In addition, treatment with FE 999011 stabilized food and water intake to prediabetic levels and reduced hypertriglyceridemia while preventing the rise in circulating free fatty acids. At the end of treatment, basal plasma GLP-1 levels were increased, and pancreatic gene expression for GLP-1 receptor was significantly upregulated. This study demonstrates that DPP-IV inhibitors such as FE 999011 could be of clinical

value to delay the progression from impaired glucose tolerance to type 2 diabetes .

L61 ANSWER 8 OF 12 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2000261281 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10799317
TITLE: Fenofibrate and rosiglitazone lower serum triglycerides with opposing effects on body weight.
AUTHOR: Chaput E; Saladin R; Silvestre M; Edgar A D
CORPORATE SOURCE: Department of Metabolic Diseases, Laboratoire Fournier, 50, rue de Dijon, Daix, 21121, France.
SOURCE: Biochemical and biophysical research communications, (2000 May 10) Vol. 271, No. 2, pp. 445-50.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 22 Jun 2000
Last Updated on STN: 18 Mar 2003
Entered Medline: 13 Jun 2000

AB Activators of peroxisome proliferator activated receptors (PPARs) are effective drugs to improve the metabolic abnormalities linking hypertriglyceridemia to diabetes, hyperglycemia, insulin-resistance, and atherosclerosis. We compared the pharmacological profile of a PPARalpha activator, fenofibrate, and a PPARgamma activator, rosiglitazone, on serum parameters, target gene expression, and body weight gain in (fa/fa) fatty Zucker rats and db/db mice as well as their association in db/db mice. Fenofibrate faithfully modified the expression of PPARalpha responsive genes. Rosiglitazone increased adipose tissue aP2 mRNA in both models while increasing liver acyl CoA oxidase mRNA in db/db mice but not in fatty Zucker rats. Both drugs lowered serum triglycerides yet rosiglitazone markedly increased body weight gain while fenofibrate decreased body weight gain in fatty Zucker rats. KRP 297, which has been reported to be a PPARalpha and gamma co-activator, also affected serum triglycerides and insulin in fatty Zucker rats although no change in body weight gain was noted. These results serve to clearly differentiate the metabolic finality of two distinct classes of drugs, as well as their corresponding nuclear receptors, having similar effects on serum triglycerides.

L61 ANSWER 9 OF 12 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 80108314 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 526068
TITLE: DBM mice as a pharmacological model of maturity onset diabetes. Studies with metformin.
AUTHOR: Junien J L; Brohon J; Guillaume M; Sterne J
SOURCE: Archives internationales de pharmacodynamie et de therapie, (1979 Sep) Vol. 241, No. 1, pp. 165-76.
Journal code: 0405353. ISSN: 0301-4533.
PUB. COUNTRY: Belgium
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198003
ENTRY DATE: Entered STN: 15 Mar 1990

Last Updated on STN: 15 Mar 1990
Entered Medline: 24 Mar 1980

AB Hyperglycemic obese and hyperinsulinemic mice of DBM strain develop a diabetic syndrome which can be compared to human maturity onset diabetes. In this study 6 to 49 weeks old female mice were used. Hyperglycemia and concomitant obesity were observed at 9 weeks. Plasma immunoreactive insulin (IRI) was maximum at 15--20 weeks, then decreased progressively with broad individual variations. Metformin, administered at 200 mg/kg per os, ineffective dosage in normal mice, showed a strong hypoglycemic effect in younger mice (11--18 weeks) with a plasma IRI decrease and no blood lactate and liver glycogen alteration. Plasma metformin concentration curve showed an exponential elimination fitted to a one compartment model with a plasma half-life of 2.7 hours. Metformin-induced hypoglycemia was lower in older mice (23--29 weeks) and corroborated their lower initial plasma IRI. All these results are in accordance with those reported in man and show that DBM mice provide a suitable model for a better understanding of antidiabetic drugs effects.

L61 ANSWER 10 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 8

ACCESSION NUMBER: 1982:145004 BIOSIS Full-text
DOCUMENT NUMBER: PREV198273004988; BA73:4988
TITLE: HEMO GLOBIN A-I-C MEASUREMENT IN THE INVESTIGATION OF HYPO GLYCEMIC DRUGS IN MICE A STUDY WITH METFORMIN.
AUTHOR(S): JUNIEN J L [Reprint author]; WAJCMAN H
CORPORATE SOURCE: SERPA, CENT RECHERCHES LAB ARON, 116 RUE CARNOT, 92151 SURESNES, FRANCE
SOURCE: Archives Internationales de Pharmacodynamie et de Therapie, (1981) Vol. 250, No. 1, pp. 123-130.
CODEN: AIPTAK. ISSN: 0003-9780.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Hyperglycemic, obese and hyperinsulinemic mice were used as a model for studying the effect of antidiabetic drugs. Using an automatic chromatography method, the variations of Hb AIc [Hb fraction AIc] were determined in these animals, untreated and after treatment by metformin. The use of this parameter gives a better insight of the overall course of diabetes than single blood glucose determination.

L61 ANSWER 11 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1983:213887 BIOSIS Full-text
DOCUMENT NUMBER: PREV198375063887; BA75:63887
TITLE: ENDOCRINE PANCREATIC REGENERATION IN DIABETIC MOUSE AN ULTRASTRUCTURAL AND HISTO ENZYMOLOGICAL STUDY.
AUTHOR(S): CHOMETTE G [Reprint author]; STERNE J; AURIOL M; TRANBALOC P; JUNIEN J L
CORPORATE SOURCE: SERVICE D'ANATOMIE PATHOLOGIQUE DU CHU PITIE-SALPETRIERE, 83, BOULEVARD DE L'HOPITAL, F 75651 PARIS
SOURCE: Annales de Pathologie, (1981) Vol. 1, No. 1, pp. 48-58.
CODEN: ASPAD2. ISSN: 0242-6498.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: FRENCH

AB The diabetic mouse [dbm] is an experimental model of genetic diabetes. In this strain, a mild diabetic syndrome occurs after 8 or 10 wk, in association with intensive endocrine pancreatic regeneration and hyperinsulinemia. The

biological, morphological and histoenzymological features of pancreas in 33 homozygous DBM mice are compared with those of 10 normal (heterozygous) controls. Twelve of these diabetic animals are treated on and after the 8th week with a hypoglycemic drug (Metformin), which makes easier the peripheral metabolism of glucose. The age of the experimental mice is 25 or 52 wk at the time of sacrifice. In non-treated diabetic mice, hyperfunctional state of β cells is always noted. On fuschine-paraldehyde stain, these cells are almost completely degranulated. High levels of enzymatic activities are found, with a special mention for the intense positivity of glucose-6-phosphatase: this pecularity follows upon an excessive intracellular glucose in β cells and subsequent production of glucose-6-phosphatase; the acid phosphatase is also intensely positive. The ultrastructural characteristics are those of very active cells: numerous light cells with large, multinucleolated nucleus: Golgi apparatus scattered everywhere in hyaloplasm and often contiguous to coat-vesicles and rigid tubules of Golgi-endoplasmic reticulum-lysosome complex; rough endoplasmic reticulum is abnormally developed, with numerous cisternae filled with granular material. In contrast with these organelles involved in an active protein synthesis, secretory granules are scarce and often small; that may be explained either by a too quick turnover or by an anomaly in insulin synthesis. In this group, another change is very striking: the extensive insular regeneration. At first, the preexistent islets of Langerhans become hyperplastic, because of abnormal multiplication of islets cells, as already proved by isotopic studies (chick). An insular neogenesis from young canalicular cells is always conspicuous. Colonization of the islets by excretory ducts is often found in old animals. These exocrine structures, lined with numerous indifferentiated parietal cells, appear to produce new endocrine cells and to participate in active regeneration. After early administration of Metformin to these diabetic mice, a significant decrease in blood sugar level is found. But hyperinsulinemia is not reduced. Morphological anomalies compared to those of non-treated group, are almost similar, although not so intensive: hyperplasia and active neogenesis of islets, without colonization; hyperfunctional state of β cells but partial restoration of secretory granules storage. These anomalies, existing in spite of lack of severe hyperglycemia , suggest in this strain, a true hypersensitivity of β cells toward glucose. Minimum elevation of blood sugar level could also induce hyperfunctional state of β cells and regeneration of islets. Among the other endocrine cells in the islets of Langerhans, D cells are not modified. α-cells are more numerous and located not only in periphery but also in center of islets; furthermore, they appear to be hyperactive; parallel cisternae of rough endoplasmic reticulum are numerous and plenty of secretory granules are located in their secretory pole. Their possible role, by means of hepatic neoglucogenesis, in initiation of hyperglycemia in this diabetes model is suggested.

L61 ANSWER 12 OF 12 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 1981:285761 BIOSIS Full-text
DOCUMENT NUMBER: PREV198172070745; BA72:70745
TITLE: DIABETIC GLOMERULO SCLEROSIS IN THE DBM MOUSE CORRELATED STUDY BY QUANTITATIVE MORPHOLOGY IMMUNO FLUORESCENCE AND ELECTRON MICROSCOPY.
AUTHOR(S): CHOMETTE G [Reprint author]; STERNE J; AURIOL M; TRANBALOC P; JUNIEN J L
CORPORATE SOURCE: SERVICE D'ANATOMIE PATHOLOGIQUE DU CHU UITIE-SALPETRIERE, 83, BLVD DE L'HOPITAL, 75651 PARIS CEDEX 13
SOURCE: Annales d'Anatomie Pathologique, (1980) Vol. 25, No. 4, pp. 317-330.
CODEN: ANAPA2. ISSN: 0003-3871.

DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: FRENCH

AB Using an experimental model of genetic diabetes (DBM mouse) a comparison was made of the results of quantitative data obtained by light microscopy and EM (measurement of glomerular and mesangial surface areas, assessment of the thickness of the basal membrane and its irregularities) and was used to demonstrate the actual presence of glomerulosclerosis in the renal parenchyma of 31 diabetic animals. Immunofluorescent investigations in these same animals demonstrated the presence of serum proteins (in particular immunoglobulins and albumin) in the glomerulus and the tubular basal membrane. These substances transuded through the vessels as a result of increased vascular permeability. Membrane abnormalities were not a consequence of hyperglycemia. In the group 1 batch of animals in which hyperglycemia was partially reduced by glycoregulatory therapy showed the same glomerular changes. Among other factors, the possible role of hyperinsulinemia constantly present in these animals, regardless of their blood glucose level, is worthy of consideration.

***** QUERY RESULTS *****

```
=> d his l29

     (FILE 'HCAPLUS' ENTERED AT 09:37:40 ON 19 JUL 2007)
L29            5 S L26 (P) (COMBINATION# OR DOSAGE# OR DOSING OR ADMINISTER?)

=> d que l29
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L7          2862 SEA FILE=HCAPLUS ABB=ON  PLU=ON  METFORMIN/OBI
L8          2633 SEA FILE=HCAPLUS ABB=ON  PLU=ON  657-24-9/RN
L9            48 SEA FILE=HCAPLUS ABB=ON  PLU=ON  657-24-9D/RN
L10         3100 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L7 OR L8 OR L9)
L11          191 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND L5
L12         4745 SEA FILE=HCAPLUS ABB=ON  PLU=ON  STATIN/OBI
L13        11420 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12 OR L5
L14          218 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 AND L10
L17              QUE  ABB=ON  PLU=ON  HYPERGLYCEMI? OR DIABETE# METILLUS
L18              QUE  ABB=ON  PLU=ON  HYPERGLYCEMI? (2A) AGENT#
L19              QUE  ABB=ON  PLU=ON  DIABET? (2A) (TYPE 2 OR TYPE II OR T
                 YPE TWO)
L24              QUE  ABB=ON  PLU=ON  AY<2003 OR PY<2003 OR PRY<2003 OR MY
                 <2003 OR REVIEW/DT
L25           53 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L11 OR L14) AND ((L17 OR L18
                 OR L19))
L26           22 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 AND L24
L29            5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L26 (P) (COMBINATION#/OBI OR
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     (FILE 'WPIX' ENTERED AT 09:51:45 ON 19 JUL 2007)
L40            9 S L37 AND L23

=> d que l40
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L16              QUE  ABB=ON  PLU=ON  METFORMIN
L17              QUE  ABB=ON  PLU=ON  HYPERGLYCEMI? OR DIABETE# METILLUS
L18              QUE  ABB=ON  PLU=ON  HYPERGLYCEMI? (2A) AGENT#
L19              QUE  ABB=ON  PLU=ON  DIABET? (2A) (TYPE 2 OR TYPE II OR T
                 YPE TWO)
L23              QUE  ABB=ON  PLU=ON  AY<2003 OR PY<2003 OR PRY<2003
L35           45 SEA FILE=WPIX ABB=ON  PLU=ON  L15 AND L16
L36         6049 SEA FILE=WPIX ABB=ON  PLU=ON  (L17 OR L18 OR L19)
L37           22 SEA FILE=WPIX ABB=ON  PLU=ON  L35 AND L36
L40            9 SEA FILE=WPIX ABB=ON  PLU=ON  L37 AND L23


=> d his l53

     (FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU, BIOTECHNO, PASCAL, CONFSCI'
     ENTERED AT 09:56:47 ON 19 JUL 2007)
L53           29 S L51 OR L52

=> d que l53
L15              QUE  ABB=ON  PLU=ON  STATIN
L16              QUE  ABB=ON  PLU=ON  METFORMIN
L17              QUE  ABB=ON  PLU=ON  HYPERGLYCEMI? OR DIABETE# METILLUS
L18              QUE  ABB=ON  PLU=ON  HYPERGLYCEMI? (2A) AGENT#
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L19             QUE  ABB=ON  PLU=ON  DIABET? (2A) (TYPE 2 OR TYPE II OR T
                YPE TWO)
L24             QUE  ABB=ON  PLU=ON  AY<2003 OR PY<2003 OR PRY<2003 OR MY
                <2003 OR REVIEW/DT
L35          45 SEA FILE=WPIX ABB=ON  PLU=ON  L15 AND L16
L36        6049 SEA FILE=WPIX ABB=ON  PLU=ON  (L17 OR L18 OR L19)
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L47      238391 SEA L36
L48         265 SEA L46 AND L47
L49          74 SEA L48 AND L24
L51          29 SEA L49 (P) (COMBINATION# OR DOSAGE# OR DOSING OR ADMINISTER?)

L52           1 SEA L49 AND (CAPSULE# OR DRAGEE# OR GRANULE# OR POWDER# OR
                SACHET# OR TABLET# OR SUSPENSION#)
L53          29 SEA L51 OR L52


=> dup rem l29 l40 l53
PROCESSING COMPLETED FOR L29
PROCESSING COMPLETED FOR L40
PROCESSING COMPLETED FOR L53
L62          41 DUP REM L29 L40 L53 (2 DUPLICATES REMOVED)
                ANSWERS '1-5' FROM FILE HCAPLUS
                ANSWERS '6-14' FROM FILE WPIX
                ANSWERS '15-26' FROM FILE MEDLINE
                ANSWERS '27-37' FROM FILE EMBASE
                ANSWERS '38-41' FROM FILE DRUGU

=> d l62 1-5 ibib ed abs hitind

L62  ANSWER 1 OF 41  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:215673  HCAPLUS  Full-text
DOCUMENT NUMBER:          146:350367
TITLE:                    Fenofibrate: a review of its use in primary
                          dyslipidemia, the metabolic syndrome and type
                          2 diabetes mellitus
AUTHOR(S):                Keating, Gillian M.; Croom, Katherine F.
CORPORATE SOURCE:         Wolters Kluwer Heath, Auckland, N. Z.
SOURCE:                   Drugs (2007), 67(1), 121-153
                          CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER:                Adis International Ltd.
DOCUMENT TYPE:            Journal; General Review
LANGUAGE:                 English
ED   Entered STN:  28 Feb 2007
AB   A review.  Fenofibrate is a fibric acid derivative indicated for use in the
     treatment of primary hypercholesterolemia, mixed dyslipidemia and
     hypertriglyceridemia in adults who have not responded to nonpharmacol.
     measures.  Its lipid-modifying effects are mediated by activation of
     peroxisome proliferator-activated receptor-α.  Fenofibrate also has nonlipid
     (i.e. pleiotropic) effects (e.g. it reduces fibrinogen, C-reactive protein and
     uric acid levels and improves flow-mediated dilatation).  Fenofibrate improves
     lipid levels (in particular triglyceride [TG] and high-d. lipoprotein-
     cholesterol [HDL-C] levels) in patients with primary dyslipidemia.  Its lipid-
     lowering profile means that fenofibrate is particularly well suited for use in
     atherogenic dyslipidemia (characterized by high TG levels, low HDL-C levels
     and small, dense low-d. lipoprotein [LDL] particles), which is commonly seen
     in patients with the metabolic syndrome and type 2 diabetes mellitus.  Indeed,
     fenofibrate improves the components of atherogenic dyslipidemia in patients
     with these conditions, including a shift from small, dense LDL particles to
     larger, more buoyant LDL particles.  Greater improvements in lipid levels are
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seen when fenofibrate is administered in combination with an HMG-CoA reductase inhibitor (statin) or in combination with ezetimibe, compared with monotherapy with these agents. In the DAIS study, fenofibrate significantly slowed the angiog. progression of focal coronary atherosclerosis in patients with type 2 diabetes. In terms of clin. outcomes, although no significant reduction in the risk of coronary events was seen with fenofibrate in the FIELD trial in patients with type 2 diabetes, treatment was associated with a significantly reduced risk of total cardiovascular disease (CVD) events, primarily through the prevention of non-fatal myocardial infarction and coronary revascularisation. Subgroup analyses revealed significant redns. in total CVD events and coronary heart disease events in patients with no previous CVD, suggesting a potential role for primary prevention with fenofibrate in patients with early type 2 diabetes. Improvements were also seen in microvascular outcomes with fenofibrate in the FIELD trial. Fenofibrate is generally well tolerated, both as monotherapy and when administered in combination with a statin. Combination therapy with fenofibrate plus a statin appears to be associated with a low risk of rhabdomyolysis; no cases of rhabdomyolysis were reported in patients receiving such therapy in the FIELD trial. Thus, fenofibrate is a valuable lipid-lowering agent, particularly in patients with atherogenic dyslipidemia.

CC 1-0 (Pharmacology)

IT Combination chemotherapy
(ezetimibe or statin combination improved lipid-lowering efficacy of fenofibrate in metabolic syndrome and type 2 diabetes mellitus patients with atherogenic dyslipidemia)

IT Fibrates
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fenofibrate and statin combination associated with low risk of rhabdomyolysis in metabolic syndrome and type 2 diabetes mellitus patient)

IT High-density lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fenofibrate improved high-d. lipoprotein-cholesterol level in metabolic syndrome and type 2 diabetes mellitus patients with atherogenic dyslipidemia)

IT Glycerides, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fenofibrate improved triglyceride level in metabolic syndrome and type 2 diabetes mellitus patients with atherogenic dyslipidemia)

IT Cardiovascular system, disease
(fenofibrate reduced total cardiovascular disease risk through prevention of non-fatal myocardial infarction and coronary revascularization in type 2 diabetes mellitus patient)

IT Low-density lipoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fenofibrate shifted small, dense low-d. lipoprotein particle to large, more buoyant particle in metabolic syndrome and type 2 diabetes mellitus patients with atherogenic dyslipidemia)

IT Coronary artery disease
HMG-CoA reductase inhibitors
(fenofibrate significantly slowed angiog. progression of focal coronary atherosclerosis in type 2 diabetes mellitus patient)

IT Dyslipidemia
Human

Hypolipemic agents
(fenofibrate was well tolerated and effective lipid-lowering agent in metabolic syndrome and type 2 diabetes mellitus patients with atherogenic dyslipidemia)

IT Metabolic disorders
(metabolic syndrome X; fenofibrate was well tolerated and effective lipid-lowering agent in metabolic syndrome and type 2 diabetes mellitus patients with atherogenic dyslipidemia)

IT Diabetes mellitus
(non-insulin-dependent; fenofibrate was well tolerated and effective lipid-lowering agent in metabolic syndrome and type 2 diabetes mellitus patients with atherogenic dyslipidemia)

IT Muscle, disease
(rhabdomyolysis; fenofibrate and statin combination associated with low risk of rhabdomyolysis in metabolic syndrome and type 2 diabetes mellitus patient)

IT 163222-33-1, Ezetimibe
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ezetimibe combination improved lipid-lowering efficacy of fenofibrate in metabolic syndrome and type 2 diabetes mellitus patients with atherogenic dyslipidemia)

IT 657-24-9, Metformin 96829-58-2, Orlistat
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fenofibrate and statin combination associated with low risk of rhabdomyolysis in metabolic syndrome and type 2 diabetes mellitus patient)

IT 49562-28-9, Fenofibrate
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fenofibrate was well tolerated and effective lipid-lowering agent in metabolic syndrome and type 2 diabetes mellitus patients with atherogenic dyslipidemia)

IT 57-88-5, Cholesterol, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fibric acid derivative fenofibrate was well tolerated and effective lipid-lowering agent in metabolic syndrome and type 2 diabetes mellitus patients with atherogenic dyslipidemia)

IT 9028-35-7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; fenofibrate significantly slowed angiog. progression of focal coronary atherosclerosis in type 2 diabetes mellitus patient)

REFERENCE COUNT: 194 THERE ARE 194 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L62 ANSWER 2 OF 41 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:42392 HCAPLUS Full-text
DOCUMENT NUMBER: 147:44785
TITLE: Diabetes, obesity, and metabolic syndrome
AUTHOR(S): Scheen, Andre J.
CORPORATE SOURCE: Division of Diabetes, Nutrition and Metabolic Disorders Department of Medicine, Sart Tilman Hospital, Liege, Belg.
SOURCE: Nutrient-Drug Interactions (2007), 1-30. Editor(s): Meckling, Kelly Anne. CRC Press LLC: Boca Raton, Fla. CODEN: 69ITVJ; ISBN: 978-1-57444-915-0
DOCUMENT TYPE: Conference; General Review

LANGUAGE: English
ED Entered STN: 14 Jan 2007
AB A review on dietary and pharmacol. interventions in metabolic diseases, such as diabetes mellitus, obesity, and metabolic syndrome (including atherogenic dyslipidemia). Potential food-drug or nutrient-drug interactions of clin. interest in patients with these disorders are described.
CC 1-0 (Pharmacology)
IT Antidiabetic agents
Antiobesity agents
Combination chemotherapy
Diet
Human
Hypolipemic agents
(combined dietary and pharmacol. drug intervention might be effective for management of metabolic disorder in patient)
IT Diabetes mellitus
(combined dietary and pharmacol. drug intervention might be effective for management of type II diabetes mellitus in patient)
IT HMG-CoA reductase inhibitors
(combined dietary and statin drug intervention might be effective for management of metabolic disorder in patient)
IT 657-24-9, Metformin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined dietary and metformin drug intervention might be effective for management of metabolic disorder in patient)
IT 79902-63-9, Simvastatin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined dietary and simvastatin drug intervention might be effective for management of metabolic disorder in patient)
IT 9028-35-7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; combined dietary and statin drug intervention might be effective for management of metabolic disorder in patient)
REFERENCE COUNT: 177 THERE ARE 177 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L62 ANSWER 3 OF 41 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:41231 HCAPLUS Full-text
DOCUMENT NUMBER: 140:111429
TITLE: Preparation of substituted heterocyclic derivatives useful as antidiabetic and antiobesity agents
INVENTOR(S): Cheng, Peter T. W.; Chen, Sean; Devasthale, Pratik; Ding, Charles Z.; Herpin, Timothy F.; Wu, Shung; Zhang, Hao; Wang, Wei; Ye, Xiang-Yang
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 543 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004665	A2	20040115	WO 2003-US22149	20030702 <--
WO 2004004665	A3	20040325		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

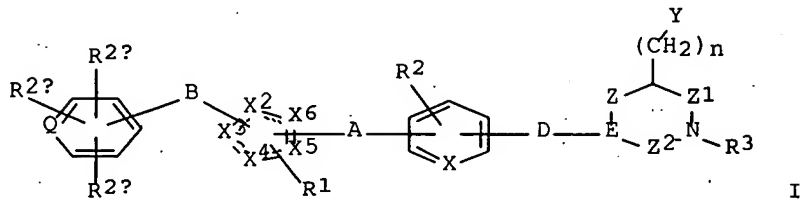
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003259131	A1	20040123	AU 2003-259131	20030702 <--
JP 2005536494	T	20051202	JP 2004-520148	20030702 <--
EP 1656368	A2	20060517	EP 2003-763485	20030702 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2004063700	A1	20040401	US 2003-616365	20030708 <--
NO 2005000077	A	20050203	NO 2005-77	20050106 <--
PRIORITY APPLN. INFO.:			US 2002-394508P P	20020709 <--
			WO 2003-US22149 W	20030702

OTHER SOURCE(S): MARPAT 140:111429

ED Entered STN: 18 Jan 2004

GI



I

AB The title compds. (I) [Z1 = (CH2)q, CO; Z2 = (CH2)p, CO; D = CH, CO, (CH2)m (where m = 0-3; p = 1, 2; q = 0-2); n = 0-2; Q = C, N; A = (CH2)x (where x = 1-5); A = (CH2)x1 (where x1 = 1-5) with an alkenyl bond or an alkynyl bond embedded anywhere in the chain; or A = -(CH2)x2-O-(CH2)x3- (where X2, X3 = 0 to 5, provided that at least one of x2 and x3 is other than 0); B = a bond or (CH2)x4 (where x4 = 1-5); X = CH, N; X2-X6 = C, N, O, or S and at least one of X2-X6 is C; R1 = H, alkyl; R2 = H, alkyl, alkoxy, halogen, (un)substituted amino; R2a, R2b, R2c = H, alkyl, alkoxy, halogen, (un)substituted amino, cyano; R3 = H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, cycloheteroalkyl, etc.; E = CH, N; Z = (CH2)x5 (where x5 is 0, i.e. a single or a double bond, 1, 2), or Z is (CH2)x6 (where x6 = 2-5), where (CH2)x6 includes an alkenyl (C:C) bond embedded within the chain or Z = -(CH2)x7-O-(CH2)x8- (where x7, x8 = 0-4); (CH2)x to (CH2)x8, (CH2)m, (CH2)n, (CH2)p and (CH2)q may be optionally substituted; Y = CO2R4 (where R4 = H, alkyl, or a prodrug ester), or Y = a C-linked 1-tetrazole, a phosphinic acid of the structure P(O)(OR4a)R5 [where R4a = H, a prodrug ester; R5 = alkyl or aryl, or a phosphonic acid of the structure P(O)(OR4a)2]] including all stereoisomers, prodrug esters, and pharmaceutically acceptable salts thereof are prepared These compds., e.g. cis-1-ethoxycarbonyl-4-[3-[2-(2- phenyl-5-methyloxazol-4-yl)ethoxy]phenyl]pyrrolidin-3-ylacetic acid and cis-1-(6-

trifluoromethylpyrimidin-2-yl)-4-[3-[2-(2-phenyl-5-methyloxazol-4-yl)ethoxy]phenyl]pyrrolidine-3-carboxylic acid, modulate serum levels of blood glucose, triglyceride, insulin, and nonesterified fatty acid (NEFA) levels, and thus are particularly useful in the treatment of diabetes and obesity, especially Type 2 diabetes, as well as hyperglycemia, hyperinsulinemia, hyperlipidemia, obesity, atherosclerosis, and related diseases employing such substituted acid derivs. alone or in combination with another antidiabetic agent and/or a hypolipidemic agent and/ or other therapeutic agents. Disclosed is a method for treating diabetes, especially Type 2 diabetes, and related diseases such as insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, hyperlipidemia, obesity, hypertriglyceridemia, inflammation, Syndrome X, diabetic complications, dysmetabolic syndrome, atherosclerosis, and related diseases, which comprises administering to a patient in need of treatment a therapeutically effective amount of the compound I. Also disclosed is a method for treating early malignant lesions (such as ductal carcinoma in situ of the breast and lobular carcinoma in situ of the breast), premalignant lesions including fibroadenoma of the breast and prostatic intraepithelial neoplasia (PIN), liposarcomas and various other epithelial tumors (including breast, prostate, colon, ovarian, gastric and lung), irritable bowel syndrome, Crohn's disease, gastric ulceritis, and osteoporosis and proliferative diseases such as psoriasis, which comprises administering to a patient in need of treatment a therapeutically effective amount of the compound I.

IC ICM A61K

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST heterocycle prepn antidiabetic antiobesity; oxazolylethoxyphenylpyrrolidineacetic acid prepn antidiabetic antiobesity; oxazolylethoxyphenylpyrimidinylpyrrolidinecarboxylic acid prepn antidiabetic antiobesity; pyrimidinylpyrrolidinecarboxylic acid oxazolylethoxyphenyl prepn antidiabetic antiobesity; pyrrolidineacetic acid oxazolylethoxyphenyl prepn antidiabetic antiobesity; hyperglycemia hyperinsulinemia hyperlipidemia obesity atherosclerosis treatment heterocycle prepn

IT Anti-inflammatory agents
Antidiabetic agents
Antiobesity agents
Antitumor agents
Antiulcer agents
Atherosclerosis
Carcinoma
Cytotoxic agents
Diabetes mellitus
Human
Hyperglycemia
Hypertriglyceridemia
Hypolipemic agents
Inflammation
Lung, neoplasm
Obesity
Osteoporosis
Ovary, neoplasm
Prostate gland, neoplasm
Psoriasis
Stomach, neoplasm
(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 50-78-2, Aspirin 51-64-9, Dexamphetamine 52-53-9, Verapamil 56-03-1, Biguanide 58-32-2, Dipyridamole 59-67-6, Niacin, biological studies 94-20-2, Chloropropamide 122-09-8, Phentermine 525-66-6, Propranolol 637-07-0, Clofibrate 657-24-9, Metformin 943-45-3D,

Fibric acid, derivs. 4205-91-8, Clonidine monohydrochloride 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 19237-84-4, Prazosin hydrochloride 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 42200-33-9, Nadolol 49562-28-9, Fenofibrate 54870-28-9, Meglitinide 55142-85-3, Ticlopidine 56180-94-0, Acarbose 62571-86-2, Captopril 72432-03-2, Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin 75847-73-3, Enalapril 76547-98-3, Lisinopril 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin 85441-61-8, Quinapril 86541-75-5, Benazepril 87333-19-5, Ramipril 89750-14-1, Glucagon-like peptide I 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 98048-97-6, Fosinopril 103775-10-6, Moexipril 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 111470-99-6, Amlodipine besylate 113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC 2993 143443-90-7, Ifetroban 144288-97-1, TS-962 144701-48-4, Telmisartan 147511-69-1, Itavastatin 152755-31-2, LY295427 159183-92-3, L750355 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 163222-33-1, Ezetimibe 166518-60-1, Avasimibe 167305-00-2, Omapatrilat 168273-06-1, Rimonabant 169319-62-4, CGS 30440 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel 196808-45-4 199113-98-9, Balaglitazone 199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677 251565-85-2, AR-H 039242 251572-86-8, P32/98 258345-41-4, GW-409544 282526-98-1, ATL-962 287714-41-4, Visastatin 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0, KAD1129 335149-23-0, NVP-DPP-728A 335149-25-2, CP331648 430433-17-3, Glipyride 444069-80-1, Axokine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (combination therapy; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

L62 ANSWER 4 OF 41 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:41224 HCAPLUS Full-text

DOCUMENT NUMBER: 140:111417

TITLE: Preparation of substituted heterocyclic derivatives useful as antidiabetic and antiobesity agents

INVENTOR(S): Cheng, Peter T. W.; Chen, Sean; Ding, Charles Z.; Herpin, Timothy F.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 160 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004655	A2	20040115	WO 2003-US21331	20030708 <--
WO 2004004655	A3	20041014		

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,

	FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2490972	A1	20040115	CA 2003-2490972		20030708 <--
AU 2003248861	A1	20040123	AU 2003-248861		20030708 <--
US 2004063762	A1	20040401	US 2003-616283		20030708 <--
US 6875782	B2	20050405			
EP 1531810	A2	20050525	EP 2003-763345		20030708 <--
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CN 1665500	A	20050907	CN 2003-816038		20030708 <--
JP 2006501187	T	20060112	JP 2004-520018		20030708 <--
NZ 537251	A	20070223	NZ 2003-537251		20030708 <--
BR 2003012503	A	20070626	BR 2003-12503		20030708 <--
NO 2004005529	A	20050203	NO 2004-5529		20041217 <--
US 2005119312	A1	20050602	US 2004-16183		20041217 <--
IN 2004DN04103	A	20070112	IN 2004-DN4103		20041222 <--
MX 2005PA00279	A	20050331	MX 2005-PA279		20050104 <--
PRIORITY APPLN. INFO.:			US 2002-394553P	P	20020709 <--
			US 2003-616283	A3	20030708
			WO 2003-US21331	W	20030708

OTHER SOURCE(S): MARPAT 140:111417
ED Entered STN: 18 Jan 2004
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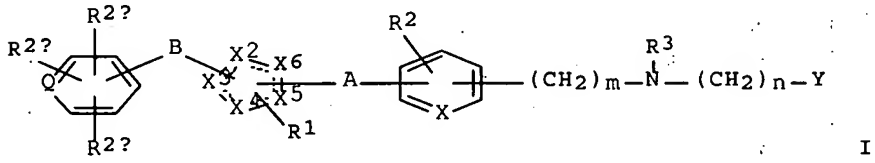

I

AB Compds. having general structure (I) [Q = C, N; A = (un)substituted (CH2)x (where x = 1-5) with an alkenyl bond or an alkynyl bond embedded anywhere in the chain, or A = (un)substituted -(CH2)x2-O-(CH2)x3- (where x2, x3 = 0-5, provided that at least one of x2 and x3 is other than 0); B = a bond, (un)substituted (CH2)x4 (where x4 = 1-5); X = CH, N; X2-X6= C, N, O, or S, provided that at least one of X2-X6 is N; and at least one of X2, X3, X4, X5 and X6 is C; R1 = H, alkyl; R2, R2a, R2b, R2c = H, alkyl, alkoxy, halogen, (un)substituted amino, cyano; R3 = H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, cycloheteroalkyl, heteroarylcarbonyl, heteroarylheteroarylalkyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, etc.; Y = CO2R (where R = H, alkyl, or a prodrug ester), or Y = a C-linked 1-tetrazole, a phosphinic acid of the structure P(O)(OR4a)R5 [where R4a = H, a prodrug ester; R5 = alkyl, aryl, or a phosphonic acid of the structure P(O)(OR4a)2]] including all stereoisomers thereof, prodrug esters thereof, and pharmaceutically acceptable salts thereof are prepared These compds. such as N-[[4-(1,2,3-triazol-4- ylmethoxy)benzyl](4-methoxypheoxycarbonyl)amino]acetic acid N-[[4-[2-(1,2,3-triazol-4-yl)ethoxy]benzyl](4-methoxypheoxycarbonyl)amino]acetic acid, N-[[1-[4-(2- or 4-imidazolylmethoxy)phenyl]isopentyl](4-methoxypheoxycarbonyl)amino]acetic acid, N-[[1-[4-(1,2,4-oxadiazol-3-ylmethoxy)phenyl]isopentyl](4-methoxypheoxycarbonyl)amino]acetic acid, N-[[4-(1,2,4-oxadiazol-3-ylmethoxy)phenethyl](isobutoxycarbonyl)amino]acetic acid derivs. modulate serum levels of blood glucose, triglyceride, insulin, and nonesterified fatty

acid (NEFA) and thus are particularly useful in the treatment of diabetes and obesity, especially Type 2 diabetes, as well as hyperglycemia, hyperinsulinemia, hyperlipidemia, obesity, atherosclerosis, and related diseases.

IC ICM A61K

CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

ST triazole imidazole oxadiazole prepn antiobesity antidiabetic; heterocycle prepn antiobesity antidiabetic; hyperglycemia hyperinsulinemia hyperlipidemia atherosclerosis treatment heterocycle prepn; triazolylmethoxybenzylmethoxypheoxycarbonylaminoacetic acid prepn antiobesity antidiabetic; triazolylethoxybenzylmethoxypheoxycarbonylaminoacetic acid prepn antiobesity antidiabetic; imidazolylmethoxyphenylisopentylmethoxypheoxycarbonylaminoacetic acid prepn antiobesity antidiabetic; oxadiazolylmethoxyphenylisopentylmethoxypheoxycarbonylaminoacetic acid prepn antiobesity antidiabetic; oxadiazolylmethoxyphenethylisobutoxycarbonylamino acetic acid prepn antiobesity antidiabetic

IT Anti-inflammatory agents
Antidiabetic agents
Antiobesity agents
Antitumor agents
Antiulcer agents
Atherosclerosis
Carcinoma
Cytotoxic agents
Diabetes mellitus
Human
Hyperglycemia
Hypertriglyceridemia
Hypolipemic agents
Inflammation
Lung, neoplasm
Neoplasm
Obesity
Osteoporosis
Ovary, neoplasm
Psoriasis
Stomach, neoplasm
(preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

IT 50-78-2, Aspirin 51-64-9, Dexamphetamine 52-53-9, Verapamil 56-03-1, Biguanide 58-32-2, Dipyridamole 59-67-6, Niacin, biological studies 94-20-2, Chloropropamide 122-09-8, Phentermine 525-66-6, Propranolol 637-07-0, Clofibrate 657-24-9, Metformin 943-45-3D, Fibric acid, derivs. 4205-91-8, Clonidine monohydrochloride 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 19237-84-4, Prazosin hydrochloride 21187-98-4, Gliclazide 21829-25-4, Nifedipine 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 42200-33-9, Nadolol 49562-28-9, Fenofibrate 54870-28-9, Meglitinide 55142-85-3, Ticlopidine 56180-94-0, Acarbose 62571-86-2, Captopril 72432-03-2, Miglitol 72956-09-3, Carvedilol 75330-75-5, Lovastatin 75847-73-3, Enalapril 76547-98-3, Lisinopril 79902-63-9, Simvastatin 80830-42-8, Fentiapril 81093-37-0, Pravastatin 85441-61-8, Quinapril 86541-75-5, Benazepril 87333-19-5, Ramipril 89750-14-1, Glucagon-like peptide I 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 98048-97-6, Fosinopril 103775-10-6, Moexipril 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 111470-99-6, Amlodipine besylate 113665-84-2, Clopidogrel 114798-26-4, Losartan 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1,

Repaglinide 137862-53-4, Valsartan 138402-11-6, Irbesartan 141758-74-9, AC 2993 143443-90-7, Ifetroban 144288-97-1, TS-962 144701-48-4, Telmisartan 147511-69-1 152755-31-2, LY295427 159183-92-3, L750355 160135-92-2, Gemopatrilat 161600-01-7, Isaglitazone 163222-33-1, Ezetimibe 166518-60-1, Avasimibe 168273-06-1, Rimonabant 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 182815-44-7, Cholestagel 196808-45-4 199113-98-9, Balaglitazone 199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677 251572-86-8, P32/98 258345-41-4, GW-409544 282526-98-1, ATL-962 287714-41-4 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0, KAD1129 335149-17-2, ARHO 39242 335149-23-0, NVP-DPP-728A 335149-25-2, CP331648 430433-17-3, Glipyride 444069-80-1, Axokine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (combination therapy; preparation of substituted heterocyclic derivs. as antidiabetic and antiobesity agents)

L62 ANSWER 5 OF 41 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:637483 HCAPLUS Full-text

DOCUMENT NUMBER: 137:185311

TITLE: Preparation of 2-aryloxy-2-arylalkanoic acids for diabetes and lipid disorders

INVENTOR(S): Adams, Alan D.; Jones, A. Brian; Berger, Joel P.; Dropinski, James F.; Elbrecht, Alexander; Liu, Kun; Macnaul, Karen Lamb; Shi, Guo-qiang; Von, Langen Derek J.; Zhou, Gaochao

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: PCT Int. Appl., 157 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002064094	A2	20020822	WO 2002-US4680		20020205 <--
WO 2002064094	A3	20030612			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2437118	A1	20020822	CA 2002-2437118		20020205 <--
AU 2002251978	A1	20020828	AU 2002-251978		20020205 <--
EP 1366012	A2	20031203	EP 2002-721022		20020205 <--
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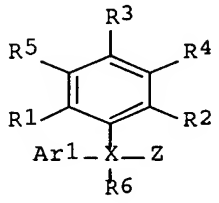
JP 2004521124	T	20040715	JP 2002-563891		20020205 <--
US 2004092596	A1	20040513	US 2003-470954		20030730 <--
US 7091230	B2	20060815			
US 2006122242	A1	20060608	US 2006-334152		20060118 <--
PRIORITY APPLN. INFO.:			US 2001-267809P	P	20010209 <--
			WO 2002-US4680	W	20020205 <--
			US 2003-470954	A3	20030730

OTHER SOURCE(S): MARPAT 137:185311
ED Entered STN: 23 Aug 2002
GI



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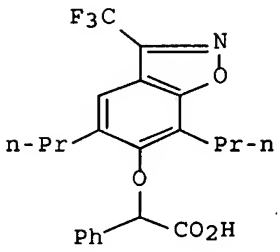

II

AB Title compds. I [R1 = halo, alkyl, alkoxy; R2 = alkyl, alicyclic; R3 = alkyl, aryl, alicyclic, heterocycle, etc.; R4 = H, OH, alkoxy, aryloxy, halo or R3-4 may be joined together to yield 5- or 6-membered heterocycle; R5 = H, halo; R6 = H, halo, CH3, CF3; Ar1 = Ph, thienyl, thiazolyl, oxazolyl, pyridyl; X = O, S; Z = COOH, tetrazole, carboxamide] were prepared For instance, 2,4-dipropylresorcinol was converted to 2,4-dihydroxy-3,5- dipropyl-α,α,α-trifluoroacetophenone (CH2Cl2, TFAA, AlCl3) and subsequently treated with i. hydroxylamine•HCl, MeOH, reflux; ii. Ac2O; iii. pyridine, reflux which afforded 5,7-dipropyl-6-hydroxy-3-trifluoromethyl-1,2-benzisoxazole. The benzisoxazole was reacted with Me 2-bromo-2-phenylacetate (DMF, Cs2CO3) and the product saponified to give II. I are potent agonists of the peroxisome proliferator activated receptor and are useful in the treatment of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR-α and/or PPAR-γ mediated diseases.

IC ICM A61K

CC 25-17 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 28, 63

IT Antioxidants
(combination pharmaceutical; preparation of 2-aryloxy-2-arylalkanoic acids for diabetes and lipid disorders)

IT Glucocorticoids
Sulfonylureas
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of 2-aryloxy-2-arylalkanoic acids for diabetes and lipid disorders)

IT Anti-inflammatory agents
(nonsteroidal, combination pharmaceutical; preparation of 2-aryloxy-2-arylalkanoic acids for diabetes and lipid disorders)

IT Alzheimer's disease
Angiogenesis
Angiogenesis inhibitors
Anti-Alzheimer's agents
Anti-inflammatory agents
Antidiabetic agents
Antiobesity agents
Atherosclerosis
Bladder, neoplasm
Cachexia
Diabetes mellitus

Human
Hypercholesterolemia
Hyperglycemia
Hypertension
Hypertriglyceridemia
Mammary gland, neoplasm
Obesity
Prostate gland, neoplasm
Psoriasis
Stomach, neoplasm
(preparation of 2-aryloxy-2-arylalkanoic acids for diabetes and lipid disorders)

IT 50-78-2, Aspirin 59-67-6, Nicotinic acid, biological studies 64-77-7, Tolbutamide 100-55-0, Nicotinyl alcohol 114-86-3, Phenformin 122-09-8, Phentermine 458-24-2, Fenfluramine 599-79-1, Azulfidine 637-07-0, Clofibrate 657-24-9, Metformin 3239-44-9, Dexfenfluramine 11041-12-6, Cholestyramine 22232-71-9, Mazindol 23288-49-5, Probucol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 41859-67-0, Bezafibrate 49562-28-9, Fenofibrate 50925-79-6, Colestipol 56180-94-0, Acarbose 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97322-87-7, Troglitazone 106650-56-0, Sibutramine 109229-58-5, Englitazone 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 143201-11-0, Rivastatin 147098-20-2, ZD-4522 147511-69-1, Itavastatin 161600-01-7, MCC-555 163222-33-1, Ezetimibe 213252-19-8, KRP-297
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination pharmaceutical; preparation of 2-aryloxy-2-arylalkanoic acids for diabetes and lipid disorders)

IT 9001-62-1, Lipase 9027-63-8, Cholesterol acyltransferase 9028-35-7, HMG-CoA reductase 9033-06-1, Glucosidase 39391-18-9, Cyclooxygenase 300865-11-6, PTP-1B
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitor, combination pharmaceutical; preparation of 2-aryloxy-2-arylalkanoic acids for diabetes and lipid disorders)

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L62 ANSWER 6 OF 41 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2007-294310 [29] WPIX
CROSS REFERENCE: 1997-044618; 1998-448966; 2002-156670
DOC. NO. CPI: C2007-108602 [29]
TITLE: Pharmaceutical composition for the prophylaxis and treatment of diabetes and diabetic complications e.g. diabetic neuropathy comprises insulin sensitivity enhancer in combination with biguanide
DERWENT CLASS: B03; B04
INVENTOR: IKEDA H; ODAKA H; SOHDA T
PATENT ASSIGNEE: (TAKE-C) TAKEDA PHARM CO LTD
COUNTRY COUNT: 18

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
EP 1764110	A1	20070321	(200729)*	EN	17[0]	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1764110 A1	Div Ex	EP 1996-304570	19960620
EP 1764110 A1		EP 2006-22352	19960620

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1764110	A1	Div ex	EP 749751	A

PRIORITY APPLN. INFO: JP 1995-153500 19950620
INT. PATENT CLASSIF.:
IPC ORIGINAL: A61K0031-155 [I,A]; A61K0031-155 [I,C]; A61K0031-4427 [I,C]; A61K0031-4439 [I,A]; A61K0045-00 [I,C]; A61K0045-06 [I,A]

BASIC ABSTRACT:

EP 1764110 A1 UPAB: 20070504

NOVELTY - A pharmaceutical composition comprises an insulin sensitivity enhancer in combination with a biguanide.

ACTIVITY - Antidiabetic; Neuroprotective; Nephrotropic; Ophthalmological; Osteopathic. No biological data given.

MECHANISM OF ACTION - Insulin sensitivity enhancer.

USE - For the manufacture of pharmaceuticals for the prophylaxis and treatment of diabetes and diabetic complications (claimed) e.g. diabetic neuropathy, nephropathy, retinopathy, macroangiopathy, osteopenia.

ADVANTAGE - The insulin sensitivity enhancer reduces the amount of a biguanide and to be administered to a diabetic patient and reduces the side effects of a biguanide. The composition shows a potent depressive effect on diabetic hyperglycemia and shows a stable hypoglycemic effect in long-term therapy with an extremely low risk of side effect. The composition is low in toxicity and can be safely used in mammals and animals.

MANUAL CODE: CPI: B06-H; B07-D04C; B07-E01; B07-F01; B10-A07D; B10-A08; B10-A17; B10-B03B; B14-F02; B14-F09; B14-J01; B14-M01C; B14-N01; B14-N03; B14-N10; B14-S04; B14-S09; B14-S18

TECH

ORGANIC CHEMISTRY - The insulin sensitivity enhancer is a compound of formula R-(Y)m-(CH2)n-CH(R1)-O-T-A-CH(L)-E1 (I) or its salt.
E1=a group of formula (ii);
R=an optionally substituted hydrocarbon or heterocyclic group (preferably optionally substituted heterocyclic group, especially pyridyl, oxazolyl or thiazolyl (all optionally mono- - trisubstituted by 1-3C alkyl, furyl, thienyl, phenyl or naphthyl);
Y=a group of formula CO, CH(OH) or NR3;
R3=optionally substituted alkyl;
m=0 or 1 (preferably 0);
n=0 - 2 (preferably 0 or 1);
X=CH or N (preferably CH);
A=bond or 1-7C divalent aliphatic hydrocarbon group (preferably bond or (CH2)2);
Q=oxygen atom or sulfur atom;
R1=hydrogen atom or an alkyl group (preferably H);
L,M = hydrogen atom; or
L+M = a bond;
T=a group of formula (i) (preferably a group of formula (ia)), in which the ring E is optionally mono - tetra-substituted and the substituents are optionally combined with R1 to form a ring;
R2=hydroxyl, acyl, amino (all optionally substituted), hydrogen atom, alkyl, halogen atom or nitro group (preferably H or 1-4C alkoxy).

PHARMACEUTICALS - Preferred Composition: The insulin sensitivity enhancer and the biguanide are administered concurrently or at staggered times to the same patient. Preferred Components: The biguanide is phenformin, metformin or buformin (preferably metformin).

ABEX WIDER DISCLOSURE - Also disclosed is a pharmaceutical composition comprising the insulin sensitivity enhancer in combination with at least one of alpha-glucosidase inhibitor, an aldose reductase inhibitor, a biguanide, a statin compound, a squalene synthesis inhibitor, a fibrate compound, a low density lipoprotein (LDL) catabolism enhancer or an angiotensin converting enzyme inhibitor.

ADMINISTRATION - The dosage of the insulin sensitivity enhancer for oral administration is 0.01 - 10 (preferably 0.05 - 10, especially 0.05 - 5) mg/kg of body weight or for parenteral administration is 0.005 - 10 (preferably 0.05 - 5, particularly 0.01 - 1) mg/kg.

SPECIFIC COMPOUNDS - Pioglitazone, pioglitazone hydrochloride and 5-((4-(2-(methyl-2-pyridylamino)ethoxy)phenyl)methyl)-2,4-thiazolidinedione are specifically claimed as the insulin sensitivity enhancers.

EXAMPLE - No suitable example is given.

L62 ANSWER 7 OF 41 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-347839 [32] WPIX
CROSS REFERENCE: 2004-282664
DOC. NO. CPI: C2004-132287 [32]
TITLE: New indole derivatives are peroxisome proliferator activated receptor agonists useful for treating type 2 diabetes mellitus
DERWENT CLASS: B02; B05
INVENTOR: ACTON J J; BLACK R M; DEBENHAM S D; LIU K; MEINKE P T; WOOD H B
PATENT ASSIGNEE: (MERI-C) MERCK & CO INC
COUNTRY COUNT: 102

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2004020408	A1	20040311	(200432)*	EN	184[0]	
AU 2003265681	A1	20040319	(200462)	EN		
NO 2005001546	A	20050524	(200545)	NO		
BR 2003013825	A	20050712	(200547)	PT		
KR 2005057074	A	20050616	(200643)	KO		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004020408	A1	WO 2003-US26677	20030827
AU 2003265681	A1	AU 2003-265681	20030827
BR 2003013825	A	BR 2003-13825	20030827
NO 2005001546	A	WO 2003-US26677	20030827
BR 2003013825	A	WO 2003-US26677	20030827
NO 2005001546	A	NO 2005-1546	20050323
KR 2005057074	A	WO 2003-US26677	20030827
KR 2005057074	A	KR 2005-703552	20050228

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 2003265681	A1	Based on	WO 2004020408	A
BR 2003013825	A	Based on	WO 2004020408	A
KR 2005057074	A	Based on	WO 2004020408	A

PRIORITY APPLN. INFO: US 2003-440672P 20030117
US 2002-406741P 20020829

INT. PATENT CLASSIF.:
MAIN: C07D209-12; C07D209-36
IPC RECLASSIF.: A61K0031-403 [I,C]; A61K0031-404 [I,A]; A61P0003-00 [I,C]; A61P0003-10 [I,A]; C07D0209-00 [I,C]; C07D0209-10 [I,A]; C07D0209-12 [I,A]; C07D0209-30 [I,A]; C07D0209-36 [I,A]; C07D0401-00 [I,C]; C07D0401-04 [I,A]; C07D0401-06 [I,A]; C07D0403-00 [I,C]; C07D0403-12 [I,A]; C07D0405-00 [I,C]; C07D0405-06 [I,A]; C07D0413-00 [I,C]; C07D0413-04 [I,A]

BASIC ABSTRACT:

WO 2004020408 A1 UPAB: 20060121

NOVELTY - Indole derivatives (I) and their salts are new.

DETAILED DESCRIPTION - Indole derivatives of formula (I) and their salts are new.

R1 = X-aryl-Y-Z or X-heteroaryl-Y-Z (optionally substituted with 1-3 groups of A);

aryl = phenyl or naphthyl;

heteroaryl = monocyclic or fused bicyclic aromatic ring structure (5-6 membered ring) containing 1-4 heteroatoms of N, O or S(O)n;

X = CH2, CH(CH3), C(CH3)2 or 3-6C cycloalkylidene;

Y = CH=CH, CH(OH)CH(OH), OCR7R8, SCR7R8 or CH2CR5R6;

Z = CO2H or tetrazole;

A = 1-4C alkyl, 1-4C alkenyl, O-1-4C alkyl or halo (all optionally substituted with 1-5 halo); either

R5-R8 = H, halo or CO2H; 1-5C alkyl, O-1-5C alkyl, 2-5C alkenyl, O-2-5C alkenyl, 3-6C cycloalkyl or phenyl (all optionally substituted with 1-5 halo) and where 3-6C cycloalkyl or phenyl are further optionally substituted with 1-3 groups selected from 1-3C alkyl or O-1-3C alkyl, and where the 1-3C alkyl or O-1-3C alkyl are optionally substituted with 1-3 halo; or

R7+R8 = 3-6C cycloalkyl optionally substituted by 1-3 halo; or when R1 is X-phenyl-Y-Z, Y is OCR7R8, R7 is H, halo, 1-5C alkyl, O-1-5C alkyl, 2-5C alkyl, O-2-5C alkyl, 3-6C cycloalkyl or phenyl, then R8 may optionally be a 1-2C bridge connected to the phenyl ring at the position ortho to Y, to form a 5-6 membered heterocyclic ring fused to the phenyl ring);

R2 = 1-4C alkyl, optionally substituted with 1-5 halo;

R3 = benzisoxazolyl, benzisothiazolyl, benzpyrazolyl, aryl, C(O) aryl, C(O)heteroaryl, Oaryl, Oheteroaryl, S(O)n aryl or S(O)n heteroaryl, (all optionally substituted with 1-3 substituent group of halo, 1-3C alkyl, O-1-3C alkyl or S-1-3C alkyl (all optionally substituted with 1-5 halo));

R4 = H or halo; 1-5C alkyl or O-1-5C alkyl (both optionally substituted with 1-5 halo);

n = 0-2; and

p = 1-3.

An INDEPENDENT CLAIM is also included for a method for treating type 2 diabetes mellitus comprising administering compound (I) optionally in combination with one or more additional antidiabetic compounds selected from metformin, sulfonylurea, insulin or DP-IV inhibitor, or with a statin selected from simvastatin, lovastatin, rosuvastatin, atorvastatin, fluvastatin, itavastatin, rivastatin and ZD-4522.

ACTIVITY - Antidiabetic.

MECHANISM OF ACTION - Peroxisome proliferator activated receptor (PPAR) agonist.

(I) were assessed for PPAR agonistic activity using transactivation assay. The median effective concentration value of (2R)-2-(3-((3-(4-

methoxybenzoyl)-2-methyl-6-(trifluoromethoxy)-1H-indol-1-yl)methyl)phenoxy)propanoic acid (Ia) was 1-3000 nM.

USE - For treating type 2 diabetes mellitus (claimed). (I) may be used alone or in combination with antidiabetic compounds or statins. MANUAL CODE: CPI: B04-J03A; B06-D01; B06-D02; B07-H; B10-A17; B14-L01; B14-S04

TECH ORGANIC CHEMISTRY - Preparation: No general methods for the preparation of (I) are given.

ABEX DEFINITIONS - Preferred Definitions: - R1 = X-phenyl-Y-Z (of formula (a)); - phenyl = optionally substituted with 1-3 groups of A; - R7, R8 = 1-3C alkyl (optionally substituted with 1-3 halo, or especially unsubstituted); - R6 = 1-3C alkyl or O-(1-3)C alkyl (both optionally substituted with 1-3 halo); - R2 = 1-3C alkyl or CF3 (preferably CH3); - X = CH(CH3), C(CH3)2 or 3-6C cycloalkylidene (preferably a bond or CH2); - Y = OCR7R8 or CH2CR5R6 (preferably OCasteriskR7R8); - Casterisk = S or R configuration; - Z = tetrazole (preferably CO2H); - q = 0-3 (preferably 0 or 1); - R3 = 3-benzisothiazolyl, 3-benzpyrazolyl, C(O) phenyl (optionally substituted by OCH3, OCF3, chloro, CF3 or CH3), O-phenyl, O-heteroaryl (especially pyridyl or quinolyl), S(O)n heteroaryl or S(O)n phenyl, preferably 3-benzisoxazolyl, aryl, C(O)phenyl, C(O)pyridyl or C(O) quinolyl (optionally substituted with 1-3 groups selected from O-1-3C alkyl or 1-3C alkyl (both optionally substituted with 1-5 halo) or halo); - n = 0-2; - A = CH3, CF3, OCH3, OCF3 or halo; - X, Y, Z = meta or para to each other; - R4 = 1-3C alkyl (preferably, CF3, OCH3, OCF3 or CH3); - p = 0 (preferably 1); - R5 = H (preferred) or 1-3C alkyl; - 1-3C alkyl = optionally substituted with 1-3 halogens.

ADMINISTRATION - Dosage of (I) is 0.1-1000 (preferably 1-50) mg/kg, administered orally, rectally, topically, parenterally, ocularly, pulmonarly or nasally.

SPECIFIC COMPOUNDS - 248 compounds (I) are specifically claimed e.g. (2R)-2-(3-((3-(4-methoxybenzoyl)-2-methyl-6-(trifluoromethoxy)-1H-indol-1-yl)methyl)phenoxy)propanoic acid (Ia).

EXAMPLE - 2-Methyl-6-trifluoromethoxyindole (645 mg), 3-bromoanisole (0.456 ml), sodium t-butoxide (404 mg), trisdibenzylidine dipalladium (206 mg) and 2-di-t-butylphosphinobiphenyl (201 mg) were stirred in toluene at 80degreesC and worked up to give 1-(3-methoxy)phenyl-2-methyl-6-trifluoromethoxyindole (a). (a) (460 mg) was dissolved in 7 ml of dichloromethane at 0degreesC. Boron tribromide (1.0 N, 2.86 ml) in dichloromethane was added and worked up to give 1-(3-hydroxy)phenyl-2-methyl-6-trifluoromethoxyindole (b). (b) (242 mg) was dissolved in methylene chloride (4 ml) and cooled to -20degreesC. A solution of diethylaluminum chloride in toluene (1.8M, 1.23 ml) was added slowly (over 1-2 minutes) and worked up to give 1-(3-hydroxy)phenyl-2-methyl-3-(4-methoxy)benzoyl-6-trifluoromethoxyindole (c). (c) (45.9 mg) was dissolved in tetrahydrofuran (0.5 ml) and cooled to 0degreesC. Triphenylphosphine (34 mg), (S)-ethyl lactate (14.7 ml), were then added and worked up to give (2R)-2-(3-(3-(4-methoxy)benzoyl-2-methyl-6-(trifluoromethoxy)-1H-indole-1-yl)phenoxy) propanoic acid ethyl ester (d). (d) (56 mg) was dissolved in ethanol (1 ml) and 25 aqueous sodium hydroxide (0.200 ml). Work-up gave (2R)-2-(3-((3-(4-methoxybenzoyl)-2-methyl-6-(trifluoromethoxy)-1H-indol-1-yl) methyl)phenoxy)propanoic acid (Ia).

L62 ANSWER 8 OF 41 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2004-098925 [10] WPIX
DOC. NO. CPI: C2004-040794 [10]
TITLE: Composition useful in the treatment of e.g. diabetes in multi-layered tablet dosage form comprises a layer-selective of prolonged release containing biguanides and layer-selective of immediate release

containing thiazolidinediones
DERWENT CLASS: A11; A96; B05; B07
INVENTOR: ANTARKAR A K; GADKARI P N; KAMDAR N M; LALA R G; SHAH J R; SHAH M J
PATENT ASSIGNEE: (THEM-N) THEMIS LAB PRIVATE LTD; (THEM-N) THEMIS LAB PVT LTD
COUNTRY COUNT: 99

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2003105809	A1	20031224	(200410)*	EN	26[0]	
AU 2002356419	A1	20031231	(200451)	EN		
EP 1515701	A1	20050323	(200521)	EN		
KR 2005016574	A	20050221	(200542)	KO		
US 20060057202	A1	20060316	(200620)	EN		
IN 2002000533	I3	20050513	(200638)	EN		
IN 2005000179	I3	20060908	(200665)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003105809	A1	WO 2002-IN207	20021014
IN 2002000533	I3	IN 2002-MU533	20020617
AU 2002356419	A1	AU 2002-356419	20021014
EP 1515701	A1	EP 2002-807523	20021014
EP 1515701	A1	WO 2002-IN207	20021014
US 20060057202	A1	WO 2002-IN207	20021014
KR 2005016574	A	KR 2004-720533	20041217
US 20060057202	A1	US 2005-518044	20050817
IN 2005000179	I3 Div Ex	IN 2002-MU533	20020617
IN 2005000179	I3	IN 2005-MU179	20050218

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002356419	A1 Based on	WO 2003105809 A
EP 1515701	A1 Based on	WO 2003105809 A

PRIORITY APPLN. INFO: IN 2002-MU533 20020617
IN 2005-MU179 20050218
INT. PATENT CLASSIF.:
MAIN: A61K009-20; A61K009-24; C07D207-30
IPC ORIGINAL: A61K0031-155 [I,A]; A61K0031-155 [I,C]; A61K0031-426 [I,A]; A61K0031-426 [I,C]; A61K0009-24 [I,A]; A61K0009-24 [I,C]
IPC RECLASSIF.: A61K0045-00 [I,C]; A61K0045-06 [I,A]; A61K0009-24 [I,A]; A61K0009-24 [I,C]

BASIC ABSTRACT:

WO 2003105809 A1 UPAB: 20060121

NOVELTY - A composition in multi-layered tablet dosage form capable of layer-selective prolonged release of at least one active pharmaceutical ingredient (API) comprising biguanides and layer-selective of immediate release of another API comprising thiazolidinediones, sulfonyl ureas, alpha-glucosidase inhibitor, aldose reductase inhibitor, statins compound, squalene synthesis inhibitor, fibrates, angiotensin converting enzymes inhibitor or low density lipoprotein (LDL) catabolism enhancers.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for preparation of multi-layered tablet dosage of composition involving screening and sizing separately prepared granules containing biguanide or its salt and (API) or their salts followed by treating with lubricants and compressing.

ACTIVITY - Antidiabetic.

MECHANISM OF ACTION - Glucose absorption inhibitor; Hepatic gluconeogenesis suppressor; Fatty acid oxidation inhibitor.

USE - For the preparation of multi-layered/bi-layered tablets useful as antihyperglycemic (claimed), especially for preventing Type 2 diabetes mellitus.

ADVANTAGE - The granules of the biguanide prolonged release layer formed can be stored for prolonged period without change in compression characteristic and can be effectively compressed into a multi-layered tablet system exhibiting pH independent prolonged release of biguanide. The bilayer tablet has hardness of 6 - 12 kg/cm2 and low friability of less than 1% without capping. The composition is patient convenient, cost effective and capable of prolonging release of one of the two drugs in a single dosage form without affecting granule characteristics. The tablet can be prepared in smaller size that is convenient to swallow than those prepared in prior art using biphasic granules. MANUAL CODE: CPI: A12-V01; B06-A01; B07-D04; B07-F01; B10-A17; B14-F09; B14-S04

TECH

PHARMACEUTICALS - Preferred Components: The biguanides are Metformin, Buformin and Phenformin or their salts (preferably Metformin hydrochloride). The thiazolidinediones are Pioglitazone, Rosiglitazone, Troglitazone or their salts (preferably Pioglitazone HCl).

Preferred Composition: The composition comprises thiazolidinediones (5 - 30 wt.%) and biguanides (1 - 10 wt.%) or Metformin HCl (500 - 2000 mg) and Pioglitazone HCl (15 - 60 mg).

Preferred Tablet: The layers of the tablet are parallel to each other, one layer is only partially covered by the next layer. The multilayer tablet is enrobed by soft gelatin ribbons for additional protection against oxidation, photodegradation, identification, ease of swallowing, taste masking and for aesthetic appeal without altering the dissolution profile.

Preferred Method: The method involves:

(1) pulverizing the biguanide e.g. Metformin HCl to particle size of less than 100 microns and comprises at least 48 (preferably over 50)% of the formulation composition;

(2) blending Metformin HCl with non-biodegradable, inert polymer in mixers such as planetary mixers, octagonal blenders, V blenders or rapid mixer granulators or fluid bed granulators;

(3) blending wet granulated API-polymer using a solvent optionally containing binders and plasticizers, in the presence of a granulation solvent such as water or hydroalcoholic solution;

(4) drying the granulated mass followed by sizing using comminuting mill such as Fitz mill or oscillating granulator or any other equipment with an appropriate mesh preferably around 1-mm mesh; and

(5) drying the granules and mixing with Talc, magnesium stearate and colloidal silicon dioxide.

The particle size of Pioglitazone HCl used is less than 30 microns. The pioglitazone HCl is blended with fillers, disintegrants, binders, lubricants and permitted colors carried out in planetary mixer, octagonal blender, double cone blender, rotary mixer granulator, drum mixer, ribbon blender, fluid bed processor or any other suitable mixer. For the preparation of the pharmaceutical compositions in multi-layered/bi-layered tablet, the nominal viscosity at 20degreesC of a 2 wt./wt.% aqueous solution of hydroxypropylmethylcellulose used is not less than 3000 cP, the nominal viscosity of a 1 wt./wt.% aqueous solution of sodium alginate at 20degreesC is not less than 50cP, the nominal viscosity of a 1 wt./wt.% aqueous dispersion of guar gum is not less than 2000 cP, the nominal

viscosity at 25degreesC of a 1 wt./wt.% aqueous solution of hydroxypropylcellulose is not less than 1500 cP; hydroxyethylcellulose is not less than 1500 cP; sodium carboxymethylcellulose is not less than 1500 cP and xanthan gum is not less than 1200 cP. The preparation of granules containing biguanide or its salt capable of being compressed to a tablet dosage form with pH independent prolonged release of biguanide at the end of 1, 4, and 8 hours lies in the range of 25 - 45%, 50 - 80% and not less than 75% respectively and that containing (API) or their salts is less than 80% at the end of 30 minutes.

POLYMERS - Preferred Components: The non-biodegradable, inert polymers are selected from cellulose derivatives, (meth)acrylic acid co-polymers, Xanthan gum, Guar gum, Alginates and/or their salts. The cellulose derivative is alkylcellulose (preferably methylcellulose or ethyl cellulose), hydroxyalkylcellulose (preferably hydroxymethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose or methylhydroxyethylcellulose) and/or carboxyalkylcellulose (preferably carboxymethylcellulose, sodium carboxymethylcellulose or calcium carboxymethylcellulose) and is incorporated in at least 35 (preferably 40 - 65) wt.% of the biguanide. The (meth)acrylic acid co-polymers are selected from esters of ethyl acrylate and methyl methacrylate, ethyl ammonium methacrylate and ethyl acrylate copolymers, ethylammonium methacrylate and methyl methacrylate copolymers, ethyl ammonium methacrylate and ethyl methacrylate copolymers, methacrylic acid and ethyl acrylate copolymers methacrylic acid and methyl methacrylate copolymers or alginate and their sodium or calcium salts. The binary combinations of the polymers are selected from combinations of hydroxypropylmethylcellulose and hydroxypropylcellulose; hydroxypropylmethylcellulose and hydroxyethylcellulose; hydroxypropylmethylcellulose and sodium carboxymethylcellulose; hydroxypropylmethylcellulose and sodium alginate; hydroxypropylmethylcellulose and Xanthan gum or hydroxypropylmethylcellulose and guar gum in the ratios of about 1:0.01 - 1:3.5. A combination of three polymers hydroxypropylmethylcellulose, sodium carboxymethylcellulose and methacrylic acid copolymer is used in ratios of 1:0.01:0.1 - 1:3.5:0.5 respectively. The disintegrating agents are selected from starch, sodium starch glycollate, crosscarmellose sodium, crosspovidone, pregelatinized starch, microcrystalline cellulose or hydroxypropylcellulose.

ABEX ADMINISTRATION - Administration of multi-layered tablet is once a day (claimed). Dosage of Metformin HCl per tablet is 250 - 2000 (preferably 500) mg and that of Pioglitazone HCl is 15 - 60 (preferably 15 - 30) mg 1 - 4 tablets/day.

EXAMPLE - A tablet composition containing prolonged release layer and immediate release layer was prepared. The prolonged release layer comprising (wt.%): metformin HCl (60), hydroxypropylmethylcellulose K4M (RTM) (37), polyvinylpyrrolidinone K30 (0.75), talc (0.5), colloidal silicon dioxide (1.5), magnesium stearate (0.25), isopropyl alcohol (qs) and purified water (qs) was prepared and compressed with an immediate release layer comprising (wt.%): pioglitazone HCl (20.05), microcrystalline cellulose (24), sodium starch glycollate (10), L-HPC (LH 21) (9), lactose (28.6), hydroxypropylmethylcellulose (1.2), talc (1.8), colloidal silicon dioxide (3.65), magnesium stearate (0.5) and lake colorant (1.2). The tablet when tested for in-vitro dissolution and drug release profile showed more than 85% of drug released after 10 minutes.

L62 ANSWER 9 OF 41 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-403290 [38] WPIX
DOC. NO. CPI: C2003-107479 [38]
TITLE: Use of leptin, its analog or derivative for treatment of metabolic abnormalities associated with lipoatrophy or

acquired form of lipoatrophy disease in human patient
DERWENT CLASS: B04
INVENTOR: DEPAOLI A M; GARG A; GARG A T S M C; ORAL E A; TAYLOR S I
PATENT ASSIGNEE: (TEXA-C) UNIV TEXAS SYSTEM; (AMGE-N) AMGEN INC; (USSH-C) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 100

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2003034996	A2	20030501	(200338)*	EN	19[4]	
EP 1444516	A2	20040811	(200452)	EN		
AU 2002359288	A1	20030506	(200460)	EN		
US 20050020496	A1	20050127	(200509)	EN		
JP 2005506994	W	20050310	(200518)	JA	66	
MX 2004003773	A1	20040801	(200548)	ES		
US 7183254	B2	20070227	(200718)	EN		
US 20070099836	A1	20070503	(200731)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003034996	A2	WO 2002-US33875	20021022
US 20050020496	A1 Provisional	US 2001-336394P	20011022
US 7183254	B2 Provisional	US 2001-336394P	20011022
AU 2002359288	A1	AU 2002-359288	20021022
EP 1444516	A2	EP 2002-793811	20021022
US 20050020496	A1 Cont of	US 2002-279129	20021022
US 7183254	B2 Cont of	US 2002-279129	20021022
EP 1444516	A2	WO 2002-US33875	20021022
JP 2005506994	W	WO 2002-US33875	20021022
MX 2004003773	A1	WO 2002-US33875	20021022
JP 2005506994	W	JP 2003-537565	20021022
US 20050020496	A1	US 2003-623189	20030718
US 7183254	B2	US 2003-623189	20030718
MX 2004003773	A1	MX 2004-3773	20040422
US 20070099836	A1 Provisional	US 2001-336394P	20011022
US 20070099836	A1 Cont of	US 2002-279129	20021022
US 20070099836	A1 Div Ex	US 2003-623189	20030718
US 20070099836	A1	US 2006-606805	20061129

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
EP 1444516	A2	Based on	WO 2003034996	A
AU 2002359288	A1	Based on	WO 2003034996	A
JP 2005506994	W	Based on	WO 2003034996	A
MX 2004003773	A1	Based on	WO 2003034996	A
US 20070099836	A1	Div ex	US 7183254	B

PRIORITY APPLN. INFO: US 2001-336394P 20011022
US 2002-279129 20021022
US 2003-623189 20030718
US 2006-606805 20061129
INT. PATENT CLASSIF.:
MAIN: A61K-00; A61K038-22
SECONDARY: A61K045-00; A61P003-04; A61P003-10; A61P043-00;

G01N033-53

IPC ORIGINAL: A61K0038-00 [I,A]; A61K0038-00 [I,C]; A61K0038-16 [I,A]; A61K0038-16 [I,C]; A61K0038-18 [I,A]; A61K0038-18 [I,C]; A61K0038-19 [I,A]; A61K0038-19 [I,C]; A61P0003-00 [I,C]; A61P0003-06 [I,A]; A61P0003-10 [I,A]; C07K0014-00 [I,A]; C07K0014-00 [I,C]; G01N0033-53 [I,A]; A61K0038-17 [I,A]; A61K0038-17 [I,C]

IPC RECLASSIF.: A61K0038-22 [I,A]; A61K0038-22 [I,C]; A61K0038-55 [I,A]; A61K0038-55 [I,C]; A61K0045-00 [I,A]; A61K0045-00 [I,C]; A61P0003-00 [I,C]; A61P0003-04 [I,A]; A61P0003-10 [I,A]; A61P0043-00 [I,A]; A61P0043-00 [I,C]; G01N0033-53 [I,A]; G01N0033-53 [I,C]; G01N0033-74 [I,A]; G01N0033-74 [I,C]

BASIC ABSTRACT:

WO 2003034996 A2 UPAB: 20060119

NOVELTY - In the treatment of metabolic abnormalities associated with lipoatrophy or acquired form of the lipoatrophy disease, a leptin (I), its analog or derivative is used.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) determination of a predisposition of a lipoatrophic patient to respond to treatment with (I), its analog or derivative involves: determining a leptin level in the patient prior to the treatment using an antibody immunoassay and then, either:

(a) ascertaining whether the leptin level is at most 4 ng/ml, or

(b) ascertaining whether the leptin level of a male patient is at most 2 ng/ml, or a female patient is at most 4 ng/ml;

(2) treatment of lipoatrophy involves a pharmaceutical regimen comprising a combination of either:

(A) (I), its analog or derivative and protease inhibitor, or

(B) (I), its analog or derivative and at least one compound selected from thiazolidinediones, fibrates, statins and metformin; and

(3) a kit for determining the predisposition of a human patient with lipoatrophy to respond to treatment with (I), its analog or derivative comprises a device for determining whether the leptin level of the patient prior to the leptin treatment is at most 2 or at most 4 ng/ml in a male or female patients respectively.

ACTIVITY - Antilipemic; Antidiabetic; Antiarteriosclerotic; Vasotropic; Anti-HIV.

MECHANISM OF ACTION - Gene therapy.

USE - For the treatment of metabolic abnormalities associated with lipoatrophy or acquired form of the lipoatrophy disease related to treat the HIV positive patient with highly active antiretroviral therapy (HAART); for determining a predisposition of a lipoatrophic patient to respond to treatment with (I), its analog or derivative (all claimed); in hormone replacement therapy in lipoatrophic patients having reduced serum concentration of leptin; in gene therapy. The metabolic abnormalities associated with lipoatrophy includes hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, vascular restenosis, and insulin resistance.

ADVANTAGE - (I) causes weight loss in obese individuals except in the state of congenital leptin deficiency and is feasible in the lipoatrophy. (I) dramatically improves glucose and triglyceride metabolism evens after all other potential therapies have been extinguished and the baseline serum concentration of leptin is less than 4 ng/ml.

MANUAL CODE: CPI: B04-C01G; B04-G01; B04-M01; B04-N02; B10-A17; B11-C04; B11-C07A; B12-K04A2; B14-F01G; B14-F06; B14-F07; B14-F10; B14-S03A; B14-S04

ABEX ADMINISTRATION - (I) is administered in a dosage of 0.02 mg/kg of body weight per day for males of all ages, about 0.03 mg/kg/day for females under 18 years and about 0.04 mg/kg/day for adult females subcutaneously,

systemically, orally, pulmonarily, nasally or transdermally.

EXAMPLE - Serum leptin concentrations of 146 HIV positive men were compared before and after highly active antiretroviral therapy (HAART). By physical examination, the men were assessed and stratified into the two major phenotypes: lipoatrophy alone and lipoatrophy with central fat gain (mixed HIV-LS). Out of the 146 men, 42 men were found to have moderate or severe lipoatrophy or lipohypertrophy in more than one body area following HAART; 27 of the 146 had lipoatrophy alone and 15 had mixed changes after HAART; and 39 out of the 146 did not have body habitus changes and these patients served as controls. The men with HIV-LS were older and had longer use of protease inhibitors. They also had lower baseline CD4 counts and had lost an average of 4 kg body weight from baseline. Before HAART, median baseline leptin levels for both the lipoatrophy and mixed groups were 3.6 ng/ml and median leptin level for the control was 4.1 ng/ml. In those who developed lipoatrophy alone after HAART, serum leptin concentration decreased significantly from 3.6 - 2.8 ng/ml. On the other hand, the serum leptin levels remained stable in both the mixed HIV-LS groups (4 ng/ml) and in the 39 HIV positive controls who did not develop HIV-LS (3.7 ng/ml). Thus the data suggest that a reduced leptin level following the (HAART) in HIV positive patients, which contributed to the development of lipoatrophy.

L62 ANSWER 10 OF 41 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-778406 [73] WPIX
DOC. NO. CPI: C2003-214184 [73]
TITLE: Dosage unit useful for treating diabetes and hyperglycemia comprises insulin secretion stimulant or antihyperglycemic biguanide compound in combination with 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitor
DERWENT CLASS: B03
INVENTOR: FREESE L M; GORHAM T R; WHEELER-DAVIS J A
PATENT ASSIGNEE: (UPSH-N) UPSHER-SMITH LAB INC
COUNTRY COUNT: 28

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
US 20030171407	A1	20030911	(200373)*	EN	9[0]	
WO 2003075933	A1	20030918	(200373)	EN		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 20030171407	A1	US 2002-94004	20020307
WO 2003075933	A1	WO 2003-US6937	20030306

PRIORITY APPLN. INFO: US 2002-94004 20020307
INT. PATENT CLASSIF.:
IPC RECLASSIF.: A61K0031-366 [I,A]; A61K0031-366 [I,C]; A61K0031-64 [I,A] ; A61K0031-64 [I,C]; A61K0045-00 [I,C]; A61K0045-06 [I,A] ; A61P0003-00 [I,C]; A61P0003-06 [I,A]; A61P0003-10 [I,A]

BASIC ABSTRACT:
US 20030171407 A1 UPAB: 20060120

NOVELTY - A pharmaceutical dosage unit comprises an insulin secretion stimulant or an antihyperglycemic biguanide compound in combination with a 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase inhibitor.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a method for reducing the number of dosages administered to a diabetic patient by utilizing a combination of active agents by:

(1) combining in a single dosage unit an insulin secretion stimulant and HMG-CoA reductase inhibitor; and

(2) administering to a diabetic patient.

ACTIVITY - Antidiabetic.

No biological data given.

MECHANISM OF ACTION - Insulin secretion stimulant; 3-Hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase inhibitor.

USE - The dosage unit is used for treating a diabetic patient (claimed), and hyperglycemia.

ADVANTAGE - At least one component of the dosage unit exhibits sustained-release properties; and the dosages required in the treatment of diabetes are less.

MANUAL CODE: CPI: B05-A01B; B06-D01; B07-A02B; B07-D02; B07-D10; B07-D12; B10-A08; B10-A17; B10-C04; B14-D05D; B14-F09; B14-S04

TECH PHARMACEUTICALS - Preferred Dosage unit: The dosage unit comprises glipizide (5-10 mg) and simvastatin (20-40 mg). Preferred Components: The insulin secretion stimulant is a sulfonylurea drug (preferably glipizide, glimepiride or glyburide, especially glipizide). The HMG-CoA reductase inhibitor is a statin drug (preferably simvastatin, atorvastatin calcium, fluvastatin sodium, lovastatin, pravastatin sodium or rosuvastatin calcium, especially simvastatin). The antihyperglycemic biguanide compound is metformin hydrochloride.

ABEX ADMINISTRATION - The dosage unit is administered orally in the form of e.g. tablet or capsule. A daily dosage for insulin secretion stimulant (e.g. glipizide) is 2.5-40 mg; dosage for HMG-CoA reductase inhibitor (e.g. simvastatin) is 5-80 mg; and dosage for antihyperglycemic biguanide compound (e.g. metformin hydrochloride) is 1500-2550 mg.

EXAMPLE - None given.

L62 ANSWER 11 OF 41 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-444013 [47] WPIX
DOC. NO. CPI: C2002-126369 [47]
TITLE: New benzopyrancarboxylic acid derivatives, useful for treating e.g. cachexia, non-insulin dependent diabetes mellitus, hyperglycemia, obesity, dyslipidemia, hypercholesterolemia or atherosclerosis
DERWENT CLASS: B02
INVENTOR: BOUERES J K; DESAI R C; KOYAMA H; MILLER D J; SAHOO S P
PATENT ASSIGNEE: (BOUE-I) BOUERES J K; (DESA-I) DESAI R C; (KOYA-I) KOYAMA H; (MERI-C) MERCK & CO INC; (MILL-I) MILLER D J; (SAHO-I) SAHOO S P
COUNTRY COUNT: 95

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC	
WO 2002026729	A2	20020404	(200247)*	EN	87[0]		<--
US 20020082292	A1	20020627	(200249)	EN			<--
AU 2001092874	A	20020408	(200252)	EN			<--
EP 1324995	A2	20030709	(200345)	EN			
US 6645997	B2	20031111	(200382)	EN			
JP 2004513090	W	20040430	(200430)	JA	158		
AU 2001292874	B2	20060615	(200705)	EN			

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002026729 A2		WO 2001-US29456	20010921
US 20020082292 A1	Provisional	US 2000-235708P	20000927
US 6645997 B2	Provisional	US 2000-235708P	20000927
US 20020082292 A1	Provisional	US 2000-244697P	20001031
US 6645997 B2	Provisional	US 2000-244697P	20001031
AU 2001092874 A		AU 2001-92874	20010921
EP 1324995 A2		EP 2001-973277	20010921
EP 1324995 A2		WO 2001-US29456	20010921
JP 2004513090 W		WO 2001-US29456	20010921
US 20020082292 A1		US 2001-961841	20010924
US 6645997 B2		US 2001-961841	20010924
JP 2004513090 W		JP 2002-531113	20010921
AU 2001292874 B2		AU 2001-292874	20010921

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 2001092874	A	Based on	WO 2002026729	A
EP 1324995	A2	Based on	WO 2002026729	A
JP 2004513090	W	Based on	WO 2002026729	A
AU 2001292874	B2	Based on	WO 2002026729	A

PRIORITY APPLN. INFO: US 2000-244697P 20001031
US 2000-235708P 20000927
US 2001-961841 20010924

INT. PATENT CLASSIF.:

MAIN: C07D311-66

SECONDARY: A61K031-353; A61K045-00; A61P001-00; A61P001-04; A61P001-18; A61P013-00; A61P013-08; A61P015-00; A61P017-00; A61P017-06; A61P017-10; A61P025-00; A61P025-28; A61P027-02; A61P029-00; A61P003-04; A61P003-06; A61P003-10; A61P035-00; A61P037-02; A61P007-00; A61P009-00; A61P009-10; A61P009-12

IPC ORIGINAL: C07D0311-00 [I,C]; C07D0311-66 [I,A]

IPC RECLASSIF.: A61K0031-352 [I,C]; A61K0031-353 [I,A]; A61K0045-00 [I,A]; A61K0045-00 [I,C]; A61P0001-00 [I,A]; A61P0001-00 [I,C]; A61P0001-04 [I,A]; A61P0001-18 [I,A]; A61P0013-00 [I,A]; A61P0013-00 [I,C]; A61P0013-08 [I,A]; A61P0015-00 [I,A]; A61P0015-00 [I,C]; A61P0017-00 [I,A]; A61P0017-00 [I,C]; A61P0017-06 [I,A]; A61P0017-10 [I,A]; A61P0025-00 [I,A]; A61P0025-00 [I,C]; A61P0025-28 [I,A]; A61P0027-00 [I,C]; A61P0027-02 [I,A]; A61P0029-00 [I,A]; A61P0029-00 [I,C]; A61P0003-00 [I,C]; A61P0003-04 [I,A]; A61P0003-06 [I,A]; A61P0003-10 [I,A]; A61P0035-00 [I,A]; A61P0035-00 [I,C]; A61P0037-00 [I,C]; A61P0037-02 [I,A]; A61P0007-00 [I,A]; A61P0007-00 [I,C]; A61P0009-00 [I,A]; A61P0009-00 [I,C]; A61P0009-10 [I,A]; A61P0009-12 [I,A]; C07D0311-00 [I,C]; C07D0311-66 [I,A]

BASIC ABSTRACT:

WO 2002026729 A2 UPAB: 20050526

NOVELTY - Benzopyran-carboxylic acid derivatives and their salts and prodrugs are new.

DETAILED DESCRIPTION - Benzopyran-carboxylic acid derivatives of formula (I) and their salts and prodrugs are new:

Z' = CH2 or CO;

R1, R2, R3, R5, R6, R7, R8, R9, R10 = e.g. H, OH, optionally substituted, optionally unsaturated alkyl or aryl;

R4 = e.g. aryloxy; and

X, Y = e.g. O, S, SO, SO2, CH2 or optionally substituted NH.

Full definitions are given in the DEFINITIONS (Full Definitions and Preferred Definitions) section. INDEPENDENT CLAIMS are included for:

(1) Compositions comprising (I) and a therapeutic agent (as below);

(2) Method for disease where insulin resistance is a component, comprises administration of (I) and a theraputic agent:

(a) insulin sensitizers:

(i) peroxisome proliferator acitvated receptor- gamma (PPARgamma) agonists, e.g. giltazones;

(ii) biguanides, e.g. metformin or phenformin;

(iii) protein tyrosine phosphatase-1B; and

(iv) dipeptidyl peptide IV inhibitors;

(b) insulin or insulin mimetics;

(c) sulfonylureas, e.g. tolbutamide or glipizide;

(d) alpha-glucosaidase inhibitors;

(e) cholesterol lowering agents;

(i) HMG-CoA reductase inhibitors;

(ii) sequestrants, e.g. cholestyramine or colestipol;

(iii) nicotinyl alcohol;

(iv) PPARalpha agonists;

(v) PPARalpha/gamma dual agonists;

(vi) inhibitors of cholesterol absorption, ezetimibe;

(vii) acyl CoA, cholesterol acetyl transferase inhibitors, e.g. avasimibe; and

(viii) anti-oxidants, e.g. probucol;

(f) PPARdelta agonists;

(g) antiobesity compounds, e.g. fenfluramine, dexfenfluramine, phenterminw, sibutramine, mazindol, orlistat, lipase inhibitors, neuropeptide Y5 inhibitors or beta-3 adrenergic receptor agonists;

(h) ileal bile acid transporter inhibitor; and

(i) inflammatory agent.

ACTIVITY - Immunomodulator; Antidiabetic; Anorectic; Antilipemic; Antiarteriosclerotic; Vasotropic; Antiinflammatory; Antiulcer; Cytostatic; Nootropic; Neuroprotective; Antipsoriatic; Antiseborrheic; Dermatological; Hypotensive.

No biological data available.

MECHANISM OF ACTION - PPARalpha agonist; PPARgamma agonist.

No biological data available.

USE - (I) are useful for treating cachexia, non-insulin dependent diabetes mellitus, hyperglycemia, impaired glucose tolerance, insulin resistance, obesity, lipid disorders, dyslipidemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, low HDL levels, high LDL levels, atherosclerosis, vascular restenosis, irritable bowel syndrome, inflammatory bowel disease, Crohn's disease, ulcerative colitis, inflammatory conditions, pancreatitis, abdominal obesity, neurodegenerative disease, retinopathy, neoplastic conditions, adipose cell tumors, adipose cell carcinomas, prostate cancer, gastric cancer, breast cancer, bladder cancer, colon cancer, angiogenesis, Alzheimer's disease, psoriasis, acne vulgaris, skin diseases modulated by PPAR, high blood pressure, syndrome X and ovarian hyperandrogenism. MANUAL CODE: CPI: B06-A01; B14-D02A2; B14-E10C; B14-F02; B14-F06;

B14-F07; B14-H01; B14-J01A2; B14-J01A4; B14-L01; B14-N13; B14-N17C; B14-S04

TECH

ORGANIC CHEMISTRY - Preparation: By reacting a substituted benzopyran carboxylate with an aryl derivative.

PHARMACEUTICALS - Preferred Therapeutic agent: The therapeutic agent is

preferably beta-hydroxy-beta-methylglutaryl (HMG) -CoA reductase inhibitor, e.g. statin. Statin is lovastatin, simvastatin, pravastatin, fluvastatin, atorvasatin, itavastatin, ZD-4522 or rivastatin.

ABEX DEFINITIONS - Full Definitions: - Z = CH2 or CO; - R1 = H, OH, 1-7C alkyl, 2-7C alkenyl, 2-7C alkynyl, 1-3C alkyloxy, 2-3C alkenyloxy, 2-3C alkynyloxy, F, Br, Cl or Ar (all optionally substituted by 1-7 of halo and/or up to 3 of 1-3C alkyloxy (optionally substituted by up to 5 of halo) or phenyl (optionally substituted by up to 3 of halo, 1-5C alkyl (optionally substituted by up to 5 of halo) or 1-3C alkyloxy (optionally substituted by up to 5 of halo)) or R1 = CR11R12 and forms a cyclopropane ring on the heterocyclic ring); - R11, R12 = H, halo, 1-5C alkyl, 2-5C alkenyl, 2-5C alkynyl, 1-3C alkyloxy, 2-3C alkenyloxy, 2-3C alkynyloxy, COOH, 1-5C alkyloxycarbonyl, 2-5C alkenyloxycarbonyl, 2-5C alkynyloxycarbonyl (all optionally substituted by up to 5 of halo and/or up to 3 of OCH3 or OCF3) or phenyl optionally substituted by up to 3 of halo, 1-5C alkyl or 1-3C alkyloxy (all optionally substituted by up to 5 of halo); - Ar = Aryl, Hetcyc, Hetaryl or Benzoheterocycle (all optionally substituted by up to 5 of halo, 1-5C alkyl, 2-5C alkenyl, 2-5C alkynyl, 1-5C alkyloxy, 2-5C alkenyloxy, 2-5C alkynyloxy, SOx-(1-5C alkyl), SOxNRaRb, SOx-phenyl, 1-3C alkylcarbonyl or CONRaRb in which each alkyl, alkenyl and alkynyl is optionally substituted by up to 5 of halo and/or up to 2 of 1-3C alkyloxy optionally substituted by up to 5 of halo and each phenyl is optionally substituted by up to 3 of halo, 1-3C alkyl or 1-3C alkoxy all optionally substituted by up to 5 of halo and in which each Hetcyc and Benzoheterocycle is optionally substituted by 3-6C spirocycloalkyl optionally substituted by up to 2 of CH3, CF3, OCH3, OCF3 or halo); - x = 0 - 2; - Aryl = 6 - 10-membered monocyclic or bicyclic aromatic system; - Hetcyc = 5- or 6-membered optionally partially unsaturated monocyclic heterocycle with 1 to 4 heteroatoms (N, S or O) in which N may optionally be NRa and S is optionally SO or SO2; - Hetaryl = 5- or 6-membered heteroaromatic ring heterocycle with 1 to 4 heteroatoms (N, S or O) in which N may optionally be NRa and S is optionally SO or SO2; - Benzoheterocycle = optionally unsaturated 5- or 6-membered heterocyclic ring (with 1 to 3 heteroatoms (N, S or O) in which N may optionally be NRa and S is optionally SO or SO2) fused to a benzene ring; - Ra, Rb = H, 1-5C alkyl, 2-5C alkenyl, 2-5C alkynyl, 1-5C alkylcarbonyl, 2-5C alkenylcarbonyl, 2-5C alkynylcarbonyl, SOx-(1-5C alkyl), SOx-phenyl, SOxNRdRe, CONRdRe, halo or phenyl in which each alkyl, alkenyl and alkynyl are optionally substituted by 1 to 5 of halo and/or 1-3 of OCH3, OCF3 or phenyl and in which the phenyl is optionally substituted by up to 3 of halo, 1-3C alkyl, 1-3C alkoxy all optionally substituted by up to 5 of halo; - Rd, Re = H, 1-5C alkyl, 2-5C alkenyl, 2-5C alkynyl or phenyl in which each alkyl, alkenyl and alkynyl are optionally substituted by 1 to 5 of halo and/or 1-3 of OCH3, OCF3 or phenyl and in which the phenyl is optionally substituted by up to 3 of halo, 1-3C alkyl, 1-3C alkoxy all optionally substituted by up to 5 of halo; - X, Y = O, S, SO, SO2, NRa or CH2; - n = 1 to 6; - R2, R3, R5, R6, R7, R8, R9, R10 = H, halo, 1-7C alkyl, 2-7C alkenyl, 2-7C alkynyl, OH, 1-5C alkyloxy, 2-5C alkenyloxy, 2-5C alkynyloxy, 1-5C alkylcarbonyl, 2-5C alkenylcarbonyl, 2-5C alkynylcarbonyl, 1-5C alkoxycarbonyl, 2-5C alkenyloxycarbonyl, 2-5C alkynyloxycarbonyl, 1-5C alkylcarbonyloxy, 2-5C alkenylcarbonyloxy, 2-5C alkynylcarbonyloxy, Ar, OAr, COAr, COOAr, OCOAr, 3-8C cycloalkyl, 3-8C cycloalkyloxy, SOx-(1-5C alkyl), SOxNRaRb, SOxAr, CONRaRb in which each alkyl, alkenyl and alkynyl is optionally substituted by up to 5 of halo, up to 2 of 1-3C alkyloxy optionally substituted by up to 5 of halo and/or Ar or 3-6C cycloalkyl; and - R4 = OAr. - Preferred Definitions: - X, Y = O; - group-X = attached at position 6- or 7- of benzopyran ring; - Z' = CH2 or C=O; - n = 2 - 4; - Ra, Rb = H or 1-5C alkyl, C(O)1-5C alkyl, S(O)x1-5C alkyl (linear or branched alkyl optionally substituted by 1-5

halo atoms) or S(O)xphenyl or phenyl (both optionally substituted by 1-3 of halo, 1-3C alkyl (optionally substituted by 1-5 halo atoms) or 1-3C alkoxy); - R1 = Cl, F or 1-4C alkyl (linear or branched and optionally substituted by 1-5 F); - R2 = Cl, Br or F; and - R3, R5, R6, R7, R8, R9, R10 = H.

ADMINISTRATION - 0.1 to 100 mg/kg/day, preferably orally, rectally, topically, parenterally, ocularly, pulmonarily or nasally.

SPECIFIC COMPOUNDS - 29 Compounds (I) are claimed, e.g. 7-(3-(4-Phenoxy-2-propyl-phenoxy)-propoxy)-chroman-2-carboxylic acid (Ia).

EXAMPLE - A suspension of ethyl 7-hydroxychromone-2-carboxylate (675.4 g) in ethanol (EtOH) (4000 ml) and concentrated hydrochloric acid (HCl) (40 ml) was hydrogenated over 5% Pd/C (68 g) at 40psi overnight. Work up gave ethyl 7-hydroxychroman-2-carboxylate (630.1 g) (a). - A mixture of (a) (100 mg), 4-(3-bromopropoxy)-3-propylphenyl phenyl ether (188 mg), cesium carbonate (Cs2CO3) (176 mg) and dimethylformamide (DMF) (3 ml) was stirred at 70degreesC for 5 hours. Work up gave ethyl 7-(3-(2-propyl-4-phenoxyphenoxy)-propoxy)-chroman-2-carboxylate (167 mg) (b). - A solution of (b) (40 mg) in 2-propanol (2 ml) and 2M sodium hydroxide (NaOH) (1 ml) was stirred at 70degreesC overnight. The mixture was concentrated and diluted with ethyl acetate (EtOAc) and 2M HCl.Work-up gave 7-(3-(4-Phenoxy-2-propyl-phenoxy)-propoxy)-chroman-2-carboxylic acid (Ia) (38 mg).

L62 ANSWER 12 OF 41 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-241560 [29] WPIX
DOC. NO. CPI: C2002-072652 [29]
TITLE: New N-substituted indoles useful in the treatment of e.g. non-insulin dependent diabetes mellitus, hyperglycemia and dyslipidemia
DERWENT CLASS: B02
INVENTOR: ACTON J J; BLACK R M; JONES A B; WOOD H B; ACTON J
PATENT ASSIGNEE: (ACTO-I) ACTON J J; (BLAC-I) BLACK R M; (JONE-I) JONES A B; (MERI-C) MERCK & CO INC; (WOOD-I) WOOD H B
COUNTRY COUNT: 94

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC	
WO 2002008188	A1	20020131	(200229)*	EN	73[0]		<--
US 20020042441	A1	20020411	(200231)	EN			<--
AU 2001077056	A	20020205	(200236)	EN			<--
US 6525083	B2	20030225	(200323)	EN			
EP 1305285	A1	20030502	(200331)	EN			
JP 2004513076	W	20040430	(200430)	JA	126		
AU 2001277056	B2	20050929	(200570)	EN			
EP 1305285	B1	20070516	(200734)	EN			
DE 60128475	E	20070628	(200743)	DE			

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002008188	A1	WO 2001-US22979	20010720
US 20020042441	A1 Provisional	US 2000-220778P	20000725
US 6525083	B2 Provisional	US 2000-220778P	20000725
AU 2001077056	A	AU 2001-77056	20010720
AU 2001277056	B2	AU 2001-277056	20010720
EP 1305285	A1	EP 2001-954836	20010720
EP 1305285	B1	EP 2001-954836	20010720

EP 1305285 A1	WO 2001-US22979 20010720
JP 2004513076 W	WO 2001-US22979 20010720
EP 1305285 B1	WO 2001-US22979 20010720
US 20020042441 A1	US 2001-912961 20010725
US 6525083 B2	US 2001-912961 20010725
JP 2004513076 W	JP 2002-514095 20010720
DE 60128475 E	DE 2001-628475 20010720
DE 60128475 E	EP 2001-954836 20010720
DE 60128475 E	WO 2001-US22979 20010720

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 2001277056	B2	Previous Publ	AU 2001277056	A
AU 2001077056	A	Based on	WO 2002008188	A
EP 1305285	A1	Based on	WO 2002008188	A
JP 2004513076	W	Based on	WO 2002008188	A
AU 2001277056	B2	Based on	WO 2002008188	A
EP 1305285	B1	Based on	WO 2002008188	A
DE 60128475	E	Based on	EP 1305285	A
DE 60128475	E	Based on	WO 2002008188	A

PRIORITY APPLN. INFO: US 2000-220778P 20000725
US 2001-912961 20010725

INT. PATENT CLASSIF.:

MAIN: C07D209-08; C07D209-28

SECONDARY: A61K031-404; A61K031-405; A61P001-00; A61P001-18; A61P017-06; A61P025-28; A61P027-02; A61P029-00; A61P003-04; A61P003-06; A61P003-10; A61P035-00; A61P009-10; A61P009-12

IPC ORIGINAL: A61K0031-403 [I,C]; A61K0031-404 [I,A]; A61K0031-405 [I,A]; A61P0003-00 [I,C]; A61P0003-10 [I,A]; C07D0209-00 [I,C]; C07D0209-08 [I,A]; C07D0209-12 [I,A]; A61K0031-403 [I,C]; A61K0031-404 [I,A]; A61K0031-405 [I,A]; A61P0003-00 [I,C]; A61P0003-10 [I,A]; C07D0209-00 [I,C]; C07D0209-08 [I,A]; C07D0209-12 [I,A]

IPC RECLASSIF.: A61K0031-403 [I,C]; A61K0031-404 [I,A]; A61P0001-00 [I,A]; A61P0001-00 [I,C]; A61P0001-18 [I,A]; A61P0017-00 [I,C]; A61P0017-06 [I,A]; A61P0025-00 [I,C]; A61P0025-28 [I,A]; A61P0027-00 [I,C]; A61P0027-02 [I,A]; A61P0029-00 [I,A]; A61P0029-00 [I,C]; A61P0003-00 [I,C]; A61P0003-04 [I,A]; A61P0003-06 [I,A]; A61P0003-10 [I,A]; A61P0035-00 [I,A]; A61P0035-00 [I,C]; A61P0009-00 [I,C]; A61P0009-10 [I,A]; A61P0009-12 [I,A]; C07D0209-00 [I,C]; C07D0209-12 [I,A]; C07D0209-28 [I,A]

BASIC ABSTRACT:

WO 2002008188 A1 UPAB: 20060119

NOVELTY - N-substituted indoles (I), their salts or prodrugs are new.

DETAILED DESCRIPTION - N-substituted indoles of formula (I), their salts or prodrugs are new.

R1 = methyl (optionally mono-, di- or tri-substituted by F);

R2 - R4 = H, halo, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 3-8C cycloalkyl, aryl, O(1-6C)alkyl, O(2-6C)alkenyl, O(2-6C)alkynyl, O-aryl, OH, S(1-6C)alkyl, S(2-6C)alkenyl, S(2-6C)alkynyl, SO2(1-6C)alkyl, SO2(2-6C)alkenyl, SO2(2-6C)alkynyl, OCON(R5)2, OCO(1-6C)alkyl or CN (where alkyl, alkenyl and alkynyl are optionally linear or branched and alkyl, alkenyl, alkynyl, cycloalkyl and aryl are optionally mono- to penta-substituted with halo, aryl, O-aryl or OMe);

R5, R6 = H, F, OH or 1-5C alkyl; or

C(R5+R6) = 3-6C cycloalkyl;
R7, R8 = H, F or 1-5C alkyl; or
R7+R8 = 3-6C cycloalkyl;
R9 = H or optionally linear or branched 1-5C alkyl;
Ar1 = phenyl, 1-naphthyl, 2-naphthyl, pyridyl or quinolyl (all mono-, di- or tri-substituted with R4);
X = C(O), S(O)2, CH2, CH(CH3), C(CH3)2, CF2 or cyclopropylidene;
Y = O or S; and
n = 0 - 5.

An INDEPENDENT CLAIM is also included for a pharmaceutical composition comprising (I), a carrier and at least one compound selected from:

(a) insulin sensitizers including:

(i) peroxisome proliferator activated receptor gamma (PPARgamma) agonists, such as glitazones (e.g. troglitazone, pioglitazone, englitazone, MCC-555 and rosiglitazone), and compounds disclosed in WO97/27857, WO97/28115, WO97/28137 and WO97/27847;

(ii) biguanides such as metformin and phenformin;

(iii) protein tyrosine phosphatase-1B (PTP-1B) inhibitors; and

(iv) dipeptidyl peptidase IV (DP-IV) inhibitors;

(b) insulin or insulin mimetics;

(c) sulfonylureas such as tolbutamide and glipizide, or related materials;

(d) alpha-glucosidase inhibitors (such as acarbose);

(e) cholesterol lowering agents such as:

(i) HMG-CoA reductase inhibitors (preferably lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin, rivastatin, itavastatin, ZD-4522 or other statins);

(ii) sequestrants (preferably cholestyramine, colestipol or dialkylaminoalkyl derivatives of a cross-linked dextran);

(iii) nicotinyl alcohol, nicotinic acid or its salt;

(iv) PPARalpha agonists such as fenofibric acid derivatives (preferably gemfibrozil, clofibrate, fenofibrate or benzafibrate);

(v) PPARalpha/gamma dual agonists, such as KRP-297;

(vi) inhibitors of cholesterol absorption, such as for example beta-sitosterol;

(vii) acyl CoA:cholesterol acyltransferase inhibitors, such as for example avasimibe, and

(viii) anti-oxidants, such as probucol;

(f) PPARdelta agonists such as those disclosed in WO97/28149;

(g) antiobesity compounds such as fenfluramine, dexfenfluramine, phentiramine, sulbitramine, orlistat, neuropeptide Y5 inhibitors, and beta3 adrenergic receptor agonists;

(h) an ileal bile acid transporter inhibitor; and

(i) agents intended for use in inflammatory conditions such as aspirin, non-steroidal anti-inflammatory drugs, glucocorticoids, azulfidine, and cyclooxygenase- 2 selective inhibitors.

ACTIVITY - Antidiabetic; Anorectic; Antilipemic; Antiarteriosclerotic; Antiinflammatory; Antiulcer; Neuroprotective; Cytostatic; Antipsoriatic; Hypotensive; Ophthalmological; Vasotropic; Nootropic; Antitumor; Antianginal; Cardiant; Cerebroprotective.

MECHANISM OF ACTION - PPARgamma agonist.

Test details are described but no results given.

USE - For treating, controlling or preventing at least one disease, disorder or condition e.g. noninsulin dependent diabetes mellitus, hyperglycemia, low glucose tolerance, insulin resistance, obesity, lipid disorders, dyslipidemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, low HDL levels, high LDL levels, atherosclerosis and its sequelae, vascular restenosis, irritable bowel syndrome, inflammatory bowel disease including Crohn's disease and ulcerative colitis, other inflammatory conditions, pancreatitis, abdominal obesity, neurodegenerative disease,

retinopathy, neoplastic conditions, adipose cell tumors, adipose cell carcinomas, such as liposarcoma, prostate cancer and other cancers, including gastric, breast, bladder and colon cancers, angiogenesis, Alzheimer's disease, psoriasis, high blood pressure, Syndrome X, ovarian hyperandrogenism (polycystic ovarian syndrome), and other disorders where insulin resistance is a component (all claimed); for treating angina, claudication, heart attack and stroke.

ADVANTAGE - (I) is free of some of the side effects that have been found in many of the glitazones.

MANUAL CODE: CPI: B01-D02; B04-J03A; B06-A02; B06-D01; B06-D02; B07-A02B; B07-A03; B07-D02; B07-D04C; B07-D10; B07-D12; B07-F01; B10-A08; B10-A17; B10-A22; B10-B01B; B10-B02G; B10-B02H; B10-B04B; B10-E02; B14-D02A2; B14-D05; B14-D05C; B14-D06; B14-E10C; B14-F01; B14-F01B; B14-F01D; B14-F01G; B14-F02B; B14-F02D1; B14-F02F2; B14-F06; B14-F07; B14-H01; B14-J01; B14-J01A4; B14-L01; B14-L06; B14-N03; B14-N13; B14-N16; B14-N17; B14-S04

TECH

ORGANIC CHEMISTRY - Preparation: No general preparation of (I) is given.

ABEX ADMINISTRATION - The composition is administered orally, rectally, topically, parenterally (including subcutaneously, intramuscularly or intravenously), ocularly (including ophthalmically), pulmonarily (including nasal or buccal inhalation), intranasally in a daily dosage of 0.1 - 100 mg/kg of animal body weight for 2 - 6 times a day in a single or divided dosage. For mammals the dosage is 1 - 1000 (preferably 1 - 50) mg.

SPECIFIC COMPOUNDS - 31 Compounds (I) are specifically claimed, e.g. (2S)-2-(3-((1-(4-methoxybenzoyl)-2-methyl-5-(trifluoromethoxy)-1H-indol-3-yl)methyl)phenoxy)propanoic acid (Ia).

EXAMPLE - 3-Hydroxybenzaldehyde (4 g) was dissolved in tetrahydrofuran (THF) (165 ml) and 1-triphenylphosphoranylidene-2-propanone (20.9 g) was added. The solution was then refluxed and chromatographed to obtain (3E)-4-(3-hydroxyphenyl)-3-buten-2-one (a). (a) (2 g) was dissolved in ethyl acetate (120 ml), 10% palladium on activated charcoal (200 mg) was then added and the vessel was evacuated and then charged with H2 for 1 hour. The mixture was filtered and filtrate was evaporated to obtain 4-(3-hydroxyphenyl)-2-butanone (b). Para-trifluoromethoxyphenyl hydrazine hydrochloride (2.58 g) and (b) (1.86 g) were stirred in acetic acid at 110 degrees C for 45 minutes. The acetic acid was then evaporated and the residue was chromatographed to obtain 3-((2-methyl-5-(trifluoromethoxy)-1H-indol-3-yl)methyl)phenol (c). (c) (50 mg) was dissolved in dichloromethane (2 ml) and to it was added (s)-allyl lactate (24 mg), triphenyl phosphine (50 mg) and diethylazodicarboxylate (0.03 ml). The mixture was then chromatographed to obtain allyl (2S)-2-(3-((2-methyl-5-(trifluoromethoxy)-1H-indol-3-yl)methyl)phenoxy)propanoate (d). (d) (467 mg) was dissolved in THF (11 ml) and cooled to -78 degrees C. Sodium bis(trimethylsilyl)amide (1.3 ml of a 1N solution in THF) was added and stirred for 10 minutes. Para-anisoyl chloride (221 mg) was then added, warmed to 0 degrees C and then the reaction was worked up to give allyl(2S)-2-(3-((1-(4-methoxybenzoyl)-2-methyl-5-(trifluoromethoxy)-1H-indol-3-yl)methyl)phenoxy)propanoate (e). (e) (490 mg) was dissolved in dimethylformamide (9 ml). 5,5-Dimethyl-1,3-cyclohexanedione (181 mg), N,N-diisopropylethylamine (0.225 ml) and (tetrakistriphenylphosphine) palladium (50 mg) were then added and the solution was stirred for 2 hours. After work up 395 mg of (2S)-2-(3-((1-(4-methoxybenzoyl)-2-methyl-5-(trifluoromethoxy)-1H-indol-3-yl)methyl)phenoxy)propanoic acid (Ia) was obtained in 87% yield.

L62 ANSWER 13 OF 41 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-594408 [56] WPIX
DOC. NO. CPI: C2000-177569 [56]

TITLE: Dietary supplements used to treat diabetes mellitus, hyperlipidemia, obesity and hypercholesterolemia and to reduce blood glucose in acute stress, comprise stabilized, reduced bicyclo(3.3.1)-nonene derivatives
DERWENT CLASS: B05
INVENTOR: ARSLANIAN R L; FORT D M; INMAN W D
PATENT ASSIGNEE: (SHAM-N) SHAMAN PHARM INC
COUNTRY COUNT: 88

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC	
WO 2000054785	A2	20000921	(200056)*	EN	73[5]		<--
AU 2000037387	A	20001004	(200101)	EN			<--

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000054785	A2	WO 2000-US6380	20000314
AU 2000037387	A	AU 2000-37387	20000314

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000037387 A		Based on	WO 2000054785 A

PRIORITY APPLN. INFO: US 1999-270305 19990315
INT. PATENT CLASSIF.:
IPC RECLASSIF.: A61K0031-122 [I,A]; A61K0031-122 [I,C]; A61K0038-28 [I,A] ; A61K0038-28 [I,C]; A61K0045-00 [I,C]; A61K0045-06 [I,A]

BASIC ABSTRACT:

WO 2000054785 A2 UPAB: 20060117

NOVELTY - Dietary supplements comprise stabilized, reduced bicyclo(3.3.1)-nonene derivatives (I).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) stabilized extracts initially obtained from the group of plants consisting of Hypericum spp. and Clusea spp. comprising a stabilized, reduced bicyclo(3.3.1)-nonene of formula (II);

(2) methods of lowering blood glucose by administering therapeutically effective amounts of compositions comprising isolated or purified compounds (II) or of formula (III); and

(3) methods of lowering serum triglycerides by administering therapeutically effective amounts of compositions comprising isolated or purified (II) or (III).

R1 = H or oxygen;

R2 = H, oxygen or benzoyl (provided that R1 and R2 are not both oxygen);

R3 = H, benzoyl, CH3, methylhalide, 3-methylbutyl or (CH2)xCOOR4; or

R2+R3 = optionally substituted furan or pyran ring;

x = 0-2;

R4 = H or 1-3C alkyl;

R5 = H or 1-6C alkyl;

R6 = 3-methylbutyl, isobutyryl, 2-methylbutyryl or benzoyl;

R7 = 3-methylbutyl;

R8 = H, CH3, methylhalide, 4-methylpentyl or (CH2)xCOOR4;

R1', R2' = O or OH (but not both O);

R3' = H or CH3; and
a-d = single or double bonds.
ACTIVITY - Antidiabetic; antilipemic; anorectic.
MECHANISM OF ACTION - None given.
USE - The supplements are used to lower blood glucose and to lower serum triglycerides (claimed). They are used to treat diabetes mellitus and lipidemia. They may also be used as hypoglycemic agents to reduce blood glucose in situations of acute stress such as experienced by animals or patients with hyperthermia, trauma, sepsis, burns or those undergoing general anesthesia, to treat hyperglycemia associated with severe head injury, cerebral thrombosis, encephalitis and heat stroke, and as hypoglycemic agents for rare congenital metabolic glycogen storage disease associated with hyperglycemia. They may also be used to treat obesity and hypercholesterolemia.
ADVANTAGE - The supplements are particularly suited for the control of hyperglycemia in patients whose blood glucose cannot be controlled by diet alone. They are capable of lowering blood glucose levels without an accompanying increase in urine glucose levels.
DESCRIPTION OF DRAWINGS - Bar graph showing the plasma glucose levels of diabetic mice treated with varying doses of Compound 3 (20, 40 and 80 mg/kg). Blood glucose levels measured at 0, 2.5, 26, 28 and 50 hours (left to right). asteriskp less than 0.05; asteriskasteriskp less than 0.01; asteriskasteriskasteriskp less than 0.0001. MANUAL CODE: CPI: B06-A01; B06-A03; B07-H; B10-A08; B10-A17; B10-E04A; B10-F02; B14-E12; B14-F06; B14-S04

TECH
PHARMACEUTICALS - Preferred Supplements: The supplements further comprise a pharmaceutically acceptable carrier. (I) is an octohydro bicyclo(3.3.1)nonene (preferably (II) or (III)).

ABEX ADMINISTRATION - Administration may be enteral or parenteral such as oral, intramuscular, intravenous, subcutaneous, transdermal, rectal or inhalational. The dose of stabilized, reduced bicyclo(3.3.1)-nonene is 0.5-1,000 mg/kg/day (claimed). Dose is at most1,000 mg/kg/day, preferably greater than 20 mg/kg/day and less than about 500 mg/kg/day (25-350 mg/kg/day). Treatment can be repeated as needed e.g. a dosage of 40 or 80 mg/kg/day can be given in single or divided doses. Administration for the treatment of diabetes may be in combination with another antihyperglycemic agent such as sulfonylureas (e.g. acetohexamide, chlorpropamide, tolazamide, tolbutamide, glyburide, glipizide, glycazide), non-sulfonylurea insulin secretagogues, biguanides (e.g. metformin, buformin), thiazolidinediones (e.g. troglitazone, pioglitazone, rosiglitazone, ciglitazone), beta-adrenoceptor agonists, alpha-glycosidase inhibitors (e.g. acarbose, miglatol) or insulin (claimed) as well as dehydroepiandrsoterone or its conjugated sulfate ester, antiglucocorticoids, tumor necrosis factor alpha inhibitors or pramlintide, and for the treatment of hyperlipidemia may be in combination with statins (e.g. fluvastatin, lovastatin, pravastatin, simvastatin), bile acid-binding resins (e.g. colestipol, cholestyramine), nicotinic acid, probucol, beta-carotene, vitamin E or vitamin C.
SPECIFIC COMPOUNDS - Nine bicyclo(3.3.1)-nonenes are given as active compounds e.g. 4-hydroxy-1-isobutyryl-8-exo-methyl-3,5,7-tris(3-methylbutyl)-8-(4-methylpentyl)-exo-bicyclo(3.3.1)nonene-2,9-dione of formula (IIa).
EXAMPLE - Single doses of 4-hydroxy-1-isobutyryl-8-exo-methyl-3,5,7-tris(3-methylbutyl)-8-(4-methylpentyl)-exo-bicyclo(3.3.1)nonene-2,9-dione (IIa) were administered orally at dosages of 20, 40 and 80 mg/kg to db/db mice. Single doses of (IIa) (40 and 80 mg/kg) given to db/db mice at 24 and 48 hours after the initial oral administration resulted in statistically significant reductions in plasma glucose relative to vehicle controls at either 0, 2.5, 26, 28 and 50 hours or at all time points after

oral administration. Two and a half hours after initial dosing, mean glucose levels for mice dosed with 40 and 80 mg/kg of (IIa) declined 104.9 mg/dl (p=0.0013) and 80 mg/dl (p=0.0279), respectively, from the baseline value. Twenty-six hours after the initial dosing, 2 hours after the 2nd dosing, mean glucose levels for the 40 and 80 mg/kg doses declined 63.4 mg/dl (p=0.0225) and 172.3 mg/dl (p less than 0.0001), respectively, from the baseline values. Twenty-eight hours after the initial dosing, 4 hours after the 2nd dosing, mean glucose levels for the 80 mg/kg dose declined 236.8 mg/dl (p less than 0.0001) from the baseline value. Fifty hours after the initial dosing, 2 hours after the 3rd dosing, mean glucose levels for the 40 and 80 mg/kg doses declined 91.4 mg/dl (p=0.0047) and 94.8 (p=0.0029), respectively from the baseline values. Compound 3 (40 mg/kg) also showed a trend in reducing plasma glucose relative to vehicle controls at 4 hours after the 2nd doing, 28 hours after the initial oral administration. Twenty-eight hours after the initial dosing, mean glucose levels for Compound 3 suspended in citrate buffer declined 99 mg/dl (p=0.0842) from baseline. By comparison, the known hypoglycemic metformin given at 250 mg/kg lowered plasma glucose levels by approximately 134 mg/dl (p less than 0.0001) 2.5 hours after the initial dose, 119.4 mg/dl (p less than 0.0001) 26 hours after the initial dose, 165.6 mg/dl (p less than 0.0001) 28 hours after the initial dose and 138.4 mg/dl 2 hours after the 3rd dose and 40 hours after the initial dose. The antihyperglycemic effect of (IIa) at dosages of 40 and 80 mg/kg occurred in the absence of any significantly adverse effect on body weight. Body weights were not affected in animals treated during the test period. It was noted that the food intake of those animals receiving (IIa) (80 mg/kg) and metformin was less than that of the normal intake range (5-6 g/day/mouse), but recovered to normal food intake range over 24-72 hours. Dose levels of 40 and 80 mg/kg produced a statistically significant reduction in plasma glucose relative to vehicle (control).

L62 ANSWER 14 OF 41 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-602057 [57] WPIX
DOC. NO. CPI: C2000-180187 [57]
TITLE: Lowering blood glucose levels and serum triglyceride levels, useful for treating e.g. diabetes and obesity, comprises administering bicyclo(3.3.1)nonenes
DERWENT CLASS: B05
INVENTOR: FORT D M
PATENT ASSIGNEE: (SHAM-N) SHAMAN PHARM INC
COUNTRY COUNT: 88

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC	
WO 2000054760	A2	20000921	(200057)*	EN	64	[6]	<--
AU 2000037441	A	20001004	(200101)	EN			<--

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000054760	A2	WO 2000-US6624	20000314
AU 2000037441	A	AU 2000-37441	20000314

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 2000037441 A Based on WO 2000054760 A

PRIORITY APPLN. INFO: US 1999-270489 19990315
INT. PATENT CLASSIF.:
IPC RECLASSIF.: A61K0031-122 [I,A]; A61K0031-122 [I,C]; A61K0031-155 [I,A]; A61K0031-155 [I,C]; A61K0031-425 [I,A]; A61K0031-425 [I,C]; A61K0031-445 [I,A]; A61K0031-445 [I,C]; A61K0031-64 [I,A]; A61K0031-64 [I,C]; A61K0031-70 [I,A]; A61K0031-70 [I,C]; A61K0038-28 [I,A]; A61K0038-28 [I,C]; A61K0045-00 [I,C]; A61K0045-06 [I,A]

BASIC ABSTRACT:

WO 2000054760 A2 UPAB: 20050411

NOVELTY - Lowering blood glucose levels comprises administration of isolated or purified bicyclo(3.3.1)nonenes (IIA) or their salts, or an extract of Hypericum species enriched in (IIA), and lowering serum triglyceride levels comprises administering an isolated or a purified bicyclo(3.3.1)nonene (IIB).

DETAILED DESCRIPTION - Lowering blood glucose levels comprises administration of an isolated or purified bicyclo(3.3.1)nonene compounds of formula (IIA) or their salts, or of an extract of Hypericum species enriched in (IIA).

a = single or double bonds;
R1 = hydroxy or oxo;
R2 = hydroxy, oxo, or benzoyl;
provided that R1 and R2 are not both oxo;
R3 = H, methyl, halomethyl, 3-methyl-2-butenyl, or (CH2)xCOOR4; or
R2+R3= a furan or pyran ring;
R4, R5 = H or 1-6C alkyl;
R6 = 3-methyl-2-butenyl, isobutyryl, 2-methylbutyryl, or benzoyl;
x = 0-2;
R7 = 3-methyl-2-butenyl; and
R8 = H, methyl, halomethyl, 4-methyl-3-pentenyl or (CH2)xCOOR4 .

INDEPENDENT CLAIMS are also included for a method of lowering serum triglyceride levels comprising administering to a mammal an amount of an isolated or a purified bicyclo(3.3.1)nonene of formula (IIB).

R11 = as for R1, or 1-6C alkoxy;
R12 = as for R2, or 1-6C alkoxy;
provided that R11 and R12 are not both oxo;
R13 = as for R3; or
R12+R13 = as for R2+R3.

ACTIVITY - Antidiabetic; antlipemic; vulnerary; antibacterial; immunosuppressive; cerebroprotective; anorectic.

Mice genetically altered to be obese and diabetic were given 80 mg/kg of 4-hydroxy-1-isobutyryl-8-methyl-3,5,7-tris-(3-methyl-2-butenyl)- 8-(4-methyl-3-pentenyl)-exo-bicyclo(3.3.1)nonene-2,9-dione (compound 1) at 0, 24, and 48 hours. The falls in blood glucose compared to control mice, as measured at 3, 27, and 51 hours, were 164.6, 172.4, and 128.5 mg/dl respectively.

MECHANISM OF ACTION - None given.

USE - (IIA) and (IIB) are useful in both clinical and veterinary medicine. (IIA) are of use in treatment of hyperglycemic disorders, especially diabetes, particularly the non-insulin dependent type (NIDDM) (claimed); other hyperglycemic conditions include hyperthermia and heat stroke, trauma (e.g., head injury), cerebral thrombosis, encephalitis, glycogen storage disease, sepsis, burns, and general anesthesia. For these purpose, they can be given either alone, or in combination with other antihyperglycemic agents e.g. insulin. (IIB) lower triglyceride and cholesterol levels, also raise plasma HDL, and are of value in treating hyperlipidemia and obesity. (IIB) can be given either alone, or in combination with other antihyperlipidemic agents, e.g., the statins.

MANUAL CODE: CPI: B06-A01; B06-A03; B07-A02B; B07-D04C; B07-F01; B10-A08; B10-A17; B10-C02; B10-C04A; B10-E04A; B10-F02; B10-G02; B14-A01; B14-E12; B14-F06; B14-G02; B14-J01;

B14-N17B; B14-S04

TECH PHARMACEUTICALS - Preferred Compounds: (IIA) and (IIB) are of formula (II'):
R1', R2' = OH or oxo;
R3' = H or Me;
provided that R1' and R2' are not simultaneously oxo.
The compounds are preferably salts of sodium, potassium, lithium, calcium, magnesium, zinc, and iron. (IIA) have a degree of purity of at least 2.5 (preferably 5) wt.% in the extract of Hypericum species.
Preferred Method: (IIA) are administered in conjunction with another antihyperglycemic agent selected from a sulfonylurea, a non-sulfonylurea insulin secretagogue, a biguanide, a thiazolidinedione, a beta-adrenoceptor agonist, an alpha-glycosidase inhibitor and insulin. The sulfonylurea is acetohexamide, chlorpropamide, tolazamide, tolbutamide, glyburide, glypizide or glycazide; the biguanide is metformin or buformin; the thiazolidinedione is troglitazone, pioglitazone, rosiglitazone or ciglitazone; and the alpha-glycosidase inhibitor is acarbose or miglatol. (IIB) is administered in conjunction with another antihyperlipidemic agent.

ABEX ADMINISTRATION - Administration is e.g. oral, transdermal, or by injection, suppository, or inhalation. Dosage is 0.5-1000 (preferably 10-350, e.g. 40-80) mg/kg/day for hypoglycemic effect and 80-160 mg/kg/day for hypolipidemic effect.
SPECIFIC COMPOUNDS - 7 Compounds (IIA) or (IIB) and 2 of their oxidative derivatives are preferred, e.g. 4-hydroxy-1-isobutyryl-8-methyl-3,5,7-tris-(3-methyl-2-butenyl)-8-(4-methyl-3-pentenyl)-exo-bicyclo(3.3.1)nonene-2,9-dione (compound 1); and - 1-(2-methyl-1-oxopropyl)-2,12-dioxo-3,10beta-bis-(3-methyl-2-butenyl)-6beta-(1-methyl-1-hydroxyethyl)-11beta-methyl-11alpha(4-methyl-3-pentenyl)-5-oxatricyclo(6.3.1.04,8)-3-dodecene.

=> d l62 15-41 ibib ab ind

L62 ANSWER 15 OF 41 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2001634764 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11688065
TITLE: [Prevalence and therapy of vascular risk factors in hospitalized type 2 diabetic patients].
Pravalenz und Therapie von Gefassrisikofaktoren bei hospitalisierten Typ-2-Diabetikern.
AUTHOR: Henzen C; Hodel T; Lehmann B; Mosimann T; Horler U; Joss R
CORPORATE SOURCE: Medizinische Klinik Kantonsspital CH-6000 Luzern 16.. Christoph.Henzen@ksl.ch
SOURCE: Schweizerische medizinische Wochenschrift, (2000 Dec 23) Vol. 130, No. 51-52, pp. 1979-83.
Journal code: 0404401. ISSN: 0036-7672.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 5 Nov 2001
Last Updated on STN: 23 Jan 2002
Entered Medline: 7 Dec 2001

AB Type 2 diabetes mellitus is often associated with other risk factors for atherosclerotic disease, resulting in a marked increase in cardiovascular events and deaths. Combined treatment of hyperglycaemia, dyslipidaemia and

hypertension significantly decreases the frequency and severity of diabetic microvascular and macrovascular complications. In a prospective cohort study including 356 type 2 diabetic patients (= 14% of all in-patients during a 6 months' period) the prevalence and treatment of cardiovascular risk factors were determined. Hypertension was diagnosed in 54% of the diabetic patients, albuminuria in 53% and dyslipidaemia in 47%; there were 40 smokers (17%). On admission the mean HbA1c was 7.7 +/- 2.0%, the mean fasting plasma glucose 10.0 +/- 4.2 mmol/l (and 8.9 +/- 3.9 mmol/l, p = 0.03, when discharged), the mean systolic blood pressure was 144 +/- 28 mm Hg (and 131 +/- 20, p < 0.0001, when discharged), and the triglycerides were 2.6 +/- 0.4 mmol/l. 34% of the hypertensive diabetic patients were treated with a combination of anti-hypertensive drugs, 44% of the dyslipidaemic diabetic patients were treated with statins, and 58% of all diabetic patients received aspirin or oral anticoagulation. 23% of the diabetic patients were treated by diet alone, 36% with insulin, 25% with sulfonylureas and 5% with metformin, while 11% were given a combination of antihyperglycaemic medication. In-hospital mortality was 11%. The diabetic patients were discharged on 2.9 +/- 1.7 different drugs. The prevalence of associated cardiovascular risk factors is high in type 2 diabetic patients, and thus a combination of drugs is often warranted. The rate of admissions and in-hospital mortality is high in type 2 diabetic patients.

CT Check Tags: Female; Male
Adult
Aged
Combined Modality Therapy
*Diabetes Mellitus, Type 2: DT, drug therapy
Diabetes Mellitus, Type 2: MO, mortality
*Diabetic Angiopathies: DT, drug therapy
Diabetic Angiopathies: MO, mortality
*Diabetic Diet
Hospital Mortality
Humans
*Hypoglycemic Agents: TU, therapeutic use
Middle Aged
*Patient Admission
Risk Factors
Switzerland

CN 0 (Hypoglycemic Agents)

L62 ANSWER 16 OF 41 MEDLINE on STN

ACCESSION NUMBER: 2007282734 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 17489673
TITLE: Treating the metabolic syndrome.
AUTHOR: Bianchi Cristina; Penno Giuseppe; Romero Fabiola; Del Prato Stefano; Miccoli Roberto
CORPORATE SOURCE: University of Pisa, Department of Endocrinology and Metabolism, Cisanello University Hospital, Pisa, Italy.. c.bianchi@ao-pisa.toscana.it
SOURCE: Expert review of cardiovascular therapy, (2007 May) Vol. 5, No. 3, pp. 491-506. Ref: 135
Journal code: 101182328. E-ISSN: 1744-8344.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200705
ENTRY DATE: Entered STN: 15 May 2007
Last Updated on STN: 30 May 2007
Entered Medline: 29 May 2007

AB The metabolic syndrome (MS), a cluster of metabolic abnormalities with insulin resistance as its central component, is increasing in prevalence and is associated with an increased risk of cardiovascular disease and Type 2 diabetes mellitus (T2DM). Current evidence supports an aggressive intervention approach that comprises lifestyle modification in conjunction with drug treatment of the MS components. Healthier eating and regular exercise greatly reduce waistline and body mass index, lower blood pressure and improve lipid profile. Lifestyle modification has been proven to prevent T2DM development. Nevertheless, appropriate treatment of MS components often requires pharmacologic intervention with insulin-sensitizing agents, such as metformin and thiazolidinediones, while statins and fibrates, or angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers are the first-line lipid-modifying or antihypertensive drugs. Only severely obese patients require specific drug treatments. Very often, drug combinations will be necessary to manage multiple risk factors. As we progress in the understanding of the pathophysiology of the MS, new targets for therapies will probably be identified and new treatments will prove to be even more efficacious than those currently available for the management of this life-threatening condition.

CT Cardiovascular Diseases: ET, etiology
Cardiovascular Diseases: PC, prevention & control
Diet
Dyslipidemias: CO, complications
Dyslipidemias: TH, therapy
Exercise
Humans
Hyperglycemia: DT, drug therapy
Insulin Resistance
*Life Style
Metabolic Syndrome X: CO, complications
*Metabolic Syndrome X: DT, drug therapy
Obesity: CO, complications
Obesity: TH, therapy

L62 ANSWER 17 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2006494816 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16918264
TITLE: Pioglitazone: an antidiabetic drug with cardiovascular therapeutic effects.
AUTHOR: Pfutzner Andreas; Schneider Christian A; Forst Thomas
CORPORATE SOURCE: IKFE - Institute for Clinical Research and Development, Parcusstr. 8 D-55116 Mainz, Germany.. AndreasP@ikfe.de
SOURCE: Expert review of cardiovascular therapy, (2006 Jul) Vol. 4, No. 4, pp. 445-59. Ref: 123
Journal code: 101182328. E-ISSN: 1744-8344.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200610
ENTRY DATE: Entered STN: 22 Aug 2006
Last Updated on STN: 7 Oct 2006
Entered Medline: 6 Oct 2006

AB The antidiabetic compound pioglitazone, an activator of the intracellular peroxisome proliferator-activated receptor-gamma, and decreases metabolic and vascular insulin resistance. The drug is well tolerated, and its metabolic effects include improvements in blood glucose and lipid control. Vascular effects consist of improvements in endothelial function and hypertension, and a reduction in surrogate markers of artherosclerosis. In a large, placebo-

controlled, outcome study in secondary prevention, PROactive study, the use of pioglitazone in addition to an existing optimized macrovascular risk management resulted in a significant reduction of macrovascular endpoints within a short observation period that was comparable to the effect of statins and angiotensin converting enzyme inhibitors in other trials. These results underline the value of pioglitazone for managing the increased cardiovascular risk of patients with a metabolic syndrome or Type 2 diabetes mellitus.

CT Body Weight: DE, drug effects
Cardiovascular Diseases: PC, prevention & control
*Cardiovascular System: DE, drug effects
Diabetes Mellitus: BL, blood
Diabetes Mellitus: DT, drug therapy
Diabetes Mellitus: PP, physiopathology
Diabetic Angiopathies: DT, drug therapy
Diabetic Angiopathies: PP, physiopathology
Diabetic Angiopathies: PC, prevention & control
Drug Therapy, Combination
Endothelium, Vascular: DE, drug effects
Endothelium, Vascular: PH, physiology
Hemoglobin A, Glycosylated: AN, analysis
Humans
Hypoglycemic Agents: PK, pharmacokinetics
*Hypoglycemic Agents: PD, pharmacology
Hypoglycemic Agents: TU, therapeutic use
Insulin Resistance: PH, physiology
Lipoproteins: BL, blood
Metformin: TU, therapeutic use
Obesity: EP, epidemiology
Obesity: PP, physiopathology
PPAR gamma: AI, antagonists & inhibitors
Thiazolidinediones: PK, pharmacokinetics
*Thiazolidinediones: PD, pharmacology
Thiazolidinediones: TU, therapeutic use
Treatment Outcome

RN 111025-46-8 (pioglitazone); 657-24-9 (Metformin)

CN 0 (Hemoglobin A, Glycosylated); 0 (Hypoglycemic Agents); 0 (Lipoproteins); 0 (PPAR gamma); 0 (Thiazolidinediones)

L62 ANSWER 18 OF 41 MEDLINE on STN

ACCESSION NUMBER:	2006090101 MEDLINE Full-text
DOCUMENT NUMBER:	PubMed ID: 16475962
TITLE:	Preventing type 2 diabetes in high risk patients: an overview of lifestyle and pharmacological measures.
AUTHOR:	Liberopoulos E N; Tsouli S; Mikhailidis D P; Elisaf M S
CORPORATE SOURCE:	Dept. of Clinical Biochemistry (Vascular Disease Prevention Clinics), Royal Free Hospital, Royal Free and University College School of Medicine, Pond Street, London NW3 2QG, UK.
SOURCE:	Current drug targets, (2006 Feb) Vol. 7, No. 2, pp. 211-28. Ref: 211 Journal code: 100960531. ISSN: 1389-4501.
PUB. COUNTRY:	Netherlands
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE) General Review; (REVIEW)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	200603
ENTRY DATE:	Entered STN: 15 Feb 2006 Last Updated on STN: 11 Mar 2006

Entered Medline: 10 Mar 2006

AB BACKGROUND: Type 2 diabetes mellitus (T2DM) is a common disease that is associated with an increased risk of vascular complications. The incidence of T2DM is also increasing. It follows that T2DM prevention is important. METHODS: Relevant articles (review articles, randomised studies and large cohort and case-control studies) were identified through a Medline search (up to March 2005). RESULTS: The first trials on T2DM prevention were based on lifestyle intervention. The results of these studies were impressive since they demonstrated that even a small reduction in weight could significantly reduce the incidence of T2DM. However, the main disadvantage of lifestyle measures is that they are difficult to achieve and sustain. Therefore, pharmacological interventions have also been evaluated. The results of trials using metformin, orlistat, nateglinide, acarbose, thiazolidinediones, hormone replacement therapy, statins or fibrates are either encouraging or require more extensive evaluation. In addition, studies using antihypertensive drugs (mainly angiotensin-converting enzyme inhibitors and angiotensin II receptor antagonists) showed that these drugs could also reduce the progression to T2DM in high risk individuals. CONCLUSIONS: T2DM has major quality of life and cost implications. Therefore, more research is needed to establish safe and cost effective ways to prevent this modern epidemic.

CT Anti-Obesity Agents: AD, administration & dosage
Anti-Obesity Agents: TU, therapeutic use
Antihypertensive Agents: AD, administration & dosage
Antihypertensive Agents: TU, therapeutic use
Antilipemic Agents: AD, administration & dosage
Antilipemic Agents: TU, therapeutic use
Body Weight: DE, drug effects
*Diabetes Mellitus, Type 2: PC, prevention & control
Estrogen Replacement Therapy
Humans
Hypoglycemic Agents: AD, administration & dosage
Hypoglycemic Agents: TU, therapeutic use
*Life Style
Risk

CN 0 (Anti-Obesity Agents); 0 (Antihypertensive Agents); 0 (Antilipemic Agents); 0 (Hypoglycemic Agents)

L62 ANSWER 19 OF 41 MEDLINE on STN

ACCESSION NUMBER:	2005315566 MEDLINE Full-text
DOCUMENT NUMBER:	PubMed ID: 15963007
TITLE:	Drug interactions of clinical importance with antihyperglycaemic agents: an update.
AUTHOR:	Scheen Andre J
CORPORATE SOURCE:	Division of Diabetes, Nutrition and Metabolic Disorders, Department of Medicine, CHU Sart Tilman, Liege, Belgium.. andre.scheen@chu.ulg.ac.be
SOURCE:	Drug safety : an international journal of medical toxicology and drug experience, (2005) Vol. 28, No. 7, pp. 601-31. Ref: 254 Journal code: 9002928. ISSN: 0114-5916.
PUB. COUNTRY:	New Zealand
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE) General Review; (REVIEW)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	200608
ENTRY DATE:	Entered STN: 21 Jun 2005 Last Updated on STN: 14 Dec 2005 Entered Medline: 2 Aug 2006

AB Because management of type 2 diabetes mellitus usually involves combined pharmacological therapy to obtain adequate glucose control and treatment of concurrent pathologies (especially dyslipidaemia and arterial hypertension), drug-drug interactions must be carefully considered with antihyperglycaemic drugs. Additive glucose-lowering effects have been extensively reported when combining sulphonylureas (or the new insulin secretagogues, meglitinide derivatives, i.e. nateglinide and repaglinide) with metformin, sulphonylureas (or meglitinide derivatives) with thiazolidinediones (also called glitazones) and the biguanide compound metformin with thiazolidinediones. Interest in combining alpha-glucosidase inhibitors with either sulphonylureas (or meglitinide derivatives), metformin or thiazolidinediones has also been demonstrated. These combinations result in lower glycosylated haemoglobin (HbA(1c)), fasting glucose and postprandial glucose levels than with either monotherapy. Even if modest pharmacokinetic interferences have been reported with some combinations, they do not appear to have important clinical consequences. No significant adverse effects, except a higher risk of hypoglycaemic episodes that may be attributed to better glycaemic control, occur with any combination. Challenging the classical dual therapy with sulphonylurea plus metformin, there is a recent trend to use alternative dual combinations (sulphonylurea plus thiazolidinedione or metformin plus thiazolidinedione). In addition, triple therapy with the addition of a thiazolidinedione to the metformin-sulphonylurea combination has been recently evaluated and allows glucose targets to be reached before insulin therapy is considered. This triple therapy appears to be safe, with no deleterious drug-drug interactions being reported so far.Potential interferences may also occur between glucose-lowering agents and other drugs, and such drug-drug interactions may have important clinical implications. Relevant pharmacological agents are those that are widely coadministered in diabetic patients (e.g. lipid-lowering agents, antihypertensive agents); those that have a narrow efficacy/toxicity ratio (e.g. digoxin, warfarin); or those that are known to induce (rifampicin [rifampin]) or inhibit (fluconazole) the cytochrome P450 (CYP) system. Metformin is currently a key compound in the pharmacological management of type 2 diabetes , used either alone or in combination with other antihyperglycaemics. There are no clinically relevant metabolic interactions with metformin, because this compound is not metabolised and does not inhibit the metabolism of other drugs. In contrast, sulphonylureas, meglitinide derivatives and thiazolidinediones are extensively metabolised in the liver via the CYP system and thus, may be subject to drug-drug metabolic interactions. Many HMG-CoA reductase inhibitors (statins) are also metabolised via the CYP system. Even if modest pharmacokinetic interactions may occur, it is not clear whether drug-drug interactions between oral antihyperglycaemic agents and statins may have clinical consequences regarding both efficacy and safety. In contrast, a marked pharmacokinetic interference has been reported between gemfibrozil and repaglinide and, to a lesser extent, between gemfibrozil and rosiglitazone. This leads to a drastic increase in plasma concentrations of each antihyperglycaemic agent when they are coadministered with the fibric acid derivative, and an increased risk of adverse effects.Some antihypertensive agents may favour hypoglycaemic episodes when co-prescribed with sulphonylureas or meglitinide derivatives, especially ACE inhibitors, but this effect seems to result from a pharmacodynamic drug-drug interaction rather than from a pharmacokinetic drug-drug interaction. No, or only modest, interferences have been described with glucose-lowering agents and other pharmacological compounds such as digoxin or warfarin. The effects of inducers or inhibitors of CYP isoenzymes on the metabolism and pharmacokinetics of the glucose-lowering agents of each pharmacological class has been tested. Significantly increased (with CYP inhibitors) or decreased (with CYP inducers) plasma levels of sulphonylureas, meglitinide derivatives and thiazolidinediones have been reported in healthy volunteers, and these pharmacokinetic changes may lead to enhanced or reduced glucose-lowering action, and thus hypoglycaemia or worsening of metabolic control,

respectively. In addition, some case reports have evidenced potential drug-drug interactions with various antihyperglycaemic agents that are usually associated with a higher risk of hypoglycaemia.

CT *Diabetes Mellitus, Type 2: DT, drug therapy
Drug Interactions
Drug Therapy, Combination
Humans
Hypoglycemic Agents: AE, adverse effects
Hypoglycemic Agents: PD, pharmacology
*Hypoglycemic Agents: TU, therapeutic use

CN 0 (Hypoglycemic Agents)

L62 ANSWER 20 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2005322053 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15958871
TITLE: Addressing the global cardiovascular risk of hypertension, dyslipidemia, diabetes mellitus, and the metabolic syndrome in the southeastern United States, part II: treatment recommendations for management of the global cardiovascular risk of hypertension, dyslipidemia, diabetes mellitus, and the metabolic syndrome.
AUTHOR: Bestermann William; Houston Mark C; Basile Jan; Egan Brent; Ferrario Carlos M; Lackland Dan; Hawkins Ralph G; Reed James; Rogers Philip; Wise Daniel; Moore Michael A
CORPORATE SOURCE: Consortium for Southeastern Hypertension Control, Beaufort, South Carolina, USA.
SOURCE: The American journal of the medical sciences, (2005 Jun) Vol. 329, No. 6, pp. 292-305. Ref: 109
Journal code: 0370506. ISSN: 0002-9629.
PUB. COUNTRY: United States
DOCUMENT TYPE: Conference; (CONSENSUS DEVELOPMENT CONFERENCE)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200507
ENTRY DATE: Entered STN: 24 Jun 2005
Last Updated on STN: 12 Jul 2005
Entered Medline: 11 Jul 2005

AB An aggressive global approach to screening and to the management of the metabolic syndrome is recommended to slow the growth of the syndrome throughout the United States. Prevention should begin in childhood with healthy nutrition, daily physical activity, and annual measurement of weight, height, and blood pressure beginning at 3 years of age. Such screenings will identify cardiovascular risk factors early, allow the health care provider to define global cardiovascular risk with the COSEHC Cardiovascular Risk Assessment Tool, and allow treatment of each risk factor. Lifelong lifestyle modifications and pharmacologic therapy will be required in most patients. Antihypertensive therapy for these patients should begin with an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker unless a compelling indication for another drug is present. Metformin should be considered the first drug for glucose control in the patient with type 2 diabetes. A statin should be used initially for hyperlipidemia unless contraindicated. Combinations of antihypertensive, antiglycemic, and lipid-lowering agents will often be required.

CT Adult
Antihypertensive Agents: TU, therapeutic use
Antilipemic Agents: TU, therapeutic use
Cardiovascular Diseases: ET, etiology
*Cardiovascular Diseases: PC, prevention & control

Child
Humans
Hyperlipidemias: CO, complications
*Hyperlipidemias: TH, therapy
Hypertension: CO, complications
*Hypertension: TH, therapy
Hypoglycemic Agents: TU, therapeutic use
Life Style
Metabolic Syndrome X: CO, complications
*Metabolic Syndrome X: TH, therapy
Platelet Aggregation Inhibitors: TU, therapeutic use
Risk Factors
Southeastern United States
CN 0 (Antihypertensive Agents); 0 (Antilipemic Agents); 0 (Hypoglycemic Agents); 0 (Platelet Aggregation Inhibitors)

L62 ANSWER 21 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2005569826 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16246214
TITLE: Diagnosis and management of the metabolic syndrome in obesity.
AUTHOR: Liberopoulos E N; Mikhailidis D P; Elisaf M S
CORPORATE SOURCE: Department of Clinical Biochemistry, Royal Free Hospital and University College Medical School (University of London), London, UK.
SOURCE: Obesity reviews : an official journal of the International Association for the Study of Obesity, (2005 Nov) Vol. 6, No. 4, pp. 283-96. Ref: 126
Journal code: 100897395. ISSN: 1467-7881.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200601
ENTRY DATE: Entered STN: 26 Oct 2005
Last Updated on STN: 28 Jan 2006
Entered Medline: 27 Jan 2006

AB The metabolic syndrome is a constellation of interrelated abnormalities that increase the risk for cardiovascular disease and progression to type 2 diabetes. The prevalence of this syndrome is increasing because of the 'obesity epidemic'. The National Cholesterol Education Program Adult Treatment Panel III defined practical criteria for the diagnosis of the metabolic syndrome and established the basic principles for its management. Also, the International Diabetes Federation recently proposed another definition. The metabolic syndrome is a secondary target for cardiovascular risk reduction. Clinicians should identify individuals with this condition, assess their cardiovascular risk and treat them by an aggressive and multifaceted approach. The most effective therapeutic intervention in patients with the metabolic syndrome should focus on modest weight reduction and regular physical activity. Adoption of a healthier diet and smoking cessation are necessary. Drug therapy may be needed to achieve recommended goals if therapeutic lifestyle changes are not sufficient. Low-density lipoprotein cholesterol is the primary target of therapy (new aggressive goals should be achieved). Statins are probably the drugs of choice. Fibrates and nicotinic acid are also useful options. Hypertension should be managed aggressively probably starting with an inhibitor of the renin-angiotensin system or a calcium channel blocker and adding a low dose of a thiazide diuretic if necessary. Aspirin should be administered if the cardiovascular risk is high. In the future acarbose, metformin, meglitinides and

thiazolidinediones may be used in patients with the metabolic syndrome to delay the onset of type 2 diabetes and reduce cardiovascular risk. Such an intense and multifactorial approach is likely to reverse the bad prognosis associated with the metabolic syndrome.

CT Cardiovascular Diseases: ET, etiology
Cardiovascular Diseases: PC, prevention & control
Diabetes Mellitus, Type 2: ET, etiology
Diabetes Mellitus, Type 2: PC, prevention & control
Dyslipidemias: DT, drug therapy
Humans
Hyperglycemia: DT, drug therapy
Hypertension: TH, therapy
*Metabolic Syndrome X: DI, diagnosis
*Metabolic Syndrome X: TH, therapy
*Obesity: CO, complications
Risk Assessment: MT, methods

L62 ANSWER 22 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2004253047 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15151470
TITLE: Treatment of metabolic syndrome.
AUTHOR: Wagh Arati; Stone Neil J
CORPORATE SOURCE: Departments of Endocrinology and Cardiology, Feinberg School of Medicine, Northwestern University, 211 E Chicago Avenue, 1050 Chicago, Il 60611, USA.
SOURCE: Expert review of cardiovascular therapy, (2004 Mar) Vol. 2, No. 2, pp. 213-28. Ref: 117
Journal code: 101182328. ISSN: 1477-9072.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 21 May 2004
Last Updated on STN: 13 Aug 2004
Entered Medline: 12 Aug 2004

AB The metabolic syndrome is intended to identify patients who have increased risk of diabetes and/or a cardiac event due to the deleterious effects of weight gain, sedentary lifestyle, and/or an atherogenic diet. The National Cholesterol Education Program's Adult Treatment Panel III definition uses easily measured clinical findings of increased abdominal circumference, elevated triglycerides, low high-density lipoprotein-cholesterol, elevated fasting blood glucose and/or elevated blood pressure. Three of these five are required for diagnosis. The authors also note that other definitions of metabolic syndrome focus more on insulin resistance and its key role in this syndrome. This review focuses on how treatment might affect each of the five components. Abdominal obesity can be treated with a variety of lower calorie diets along with regular exercise. Indeed, all of the five components of the metabolic syndrome are improved by even modest amounts of weight loss achieved with diet and exercise. For those with impaired fasting glucose tolerance, there is good evidence that a high fiber, low saturated fat diet with increased daily exercise can reduce the incidence of diabetes by almost 60%. Of note, subjects who exercise the most, gain the most benefit. Metformin has also been shown to be helpful in these subjects. Thiazolidinedione drugs may prove useful, but further studies are needed. Although intensified therapeutic lifestyle change will help the abnormal lipid profile, some patients may require drug therapy. This review also discusses the use of statins, fibrates, and niacin. Likewise, while hypertension in the metabolic syndrome benefits from therapeutic lifestyle change, physicians should also

consider angiotensin converting enzyme inhibitor drugs or angiotensin receptor blockers, due to their effects on preventing complications of diabetes, such as progression of diabetic nephropathy and due to their effects on regression of left ventricular hypertrophy. Aspirin should be considered in those with at least a 10% risk of a coronary event over 10 years. Finally, three related conditions, nonalcoholic fatty liver disease, polycystic ovary syndrome and protease inhibitor associated lipodystrophy improve with therapeutic lifestyle change. Although metformin is shown to be useful with polycystic ovary syndrome, the data supporting drug therapy for the other syndromes is less convincing. More robust studies are needed before any firm recommendations can be made.

CT Abdomen
Adipose Tissue
Antihypertensive Agents: AD, administration & dosage
Antilipemic Agents: AD, administration & dosage
Blood Glucose: ME, metabolism
Blood Pressure
*Caloric Restriction
Cholesterol, HDL: BL, blood
Diabetes Mellitus, Type 2: ET, etiology
*Diabetes Mellitus, Type 2: TH, therapy
Diet, Atherogenic
Diet, Reducing
*Exercise
Humans
Hyperlipidemias: ET, etiology
*Hyperlipidemias: TH, therapy
Hypertension: ET, etiology
*Hypertension: TH, therapy
Hypoglycemic Agents: AD, administration & dosage
*Life Style
Metabolic Syndrome X: DI, diagnosis
Metabolic Syndrome X: ET, etiology
Metabolic Syndrome X: PP, physiopathology
*Metabolic Syndrome X: TH, therapy
Risk Factors
Triglycerides: BL, blood
Weight Gain
Weight Loss

CN 0 (Antihypertensive Agents); 0 (Antilipemic Agents); 0 (Blood Glucose); 0 (Cholesterol, HDL); 0 (Hypoglycemic Agents); 0 (Triglycerides)

L62 ANSWER 23 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2003306325 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12833770
TITLE: The type 2 tablet. Evidence based medication for type 2 diabetes.
AUTHOR: Phillips Patrick; Braddon Jody
CORPORATE SOURCE: Queen Elizabeth Hospital and Health Service, Woodville, South Australia.. pphillips@tqeh.nwahs.sa.gov.au
SOURCE: Australian family physician, (2003 Jun) Vol. 32, No. 6, pp. 431-6. Ref: 23
Journal code: 0326701. ISSN: 0300-8495.
PUB. COUNTRY: Australia
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307

ENTRY DATE: Entered STN: 2 Jul 2003
Last Updated on STN: 30 Jul 2003
Entered Medline: 29 Jul 2003

AB BACKGROUND: Diabesity--the association of type 2 diabetes and obesity--is a major public health problem worldwide and is increasing dramatically in Australia. The abnormalities associated with diabetes, the 'type 2 diabetes syndrome' are cardiovascular risk factors and increased cardiovascular events. The full implications of type 2 diabetes syndrome may not be fully appreciated and opportunities for effective interventions may be being missed. OBJECTIVE: This article aims to review the cardiovascular risk associated with type 2 diabetes syndrome and to summarise the evidence supporting wider use of medications that target the different components of type 2 diabetes syndrome. DISCUSSION: The cardiovascular benefits of metformin, the ACE inhibitors, aspirin and the statins have been shown in prospective controlled trials and the beneficial effects of these medications are additive. There is a case for these medications to be considered for those with type 2 diabetes (and an opportunity for the pharmaceutical industry to provide the 'type 2 tablet' containing all four medications).

CT Check Tags: Male
Adult
Age Factors
Aged
*Angiotensin-Converting Enzyme Inhibitors: AD, administration & dosage
Attitude to Health
Australia
Cardiovascular Diseases: EP, epidemiology
*Cardiovascular Diseases: PC, prevention & control
Comorbidity
Diabetes Mellitus: DI, diagnosis
*Diabetes Mellitus: EP, epidemiology
Diabetes Mellitus, Type 2: DI, diagnosis
*Diabetes Mellitus, Type 2: DT, drug therapy
*Diabetes Mellitus, Type 2: EP, epidemiology
Drug Combinations
Evidence-Based Medicine
Humans
*Hypoglycemic Agents: AD, administration & dosage
Middle Aged
*Obesity
Pharmaceutical Preparations
Prognosis
Risk Factors
Sensitivity and Specificity
Severity of Illness Index

CN 0 (Angiotensin-Converting Enzyme Inhibitors); 0 (Drug Combinations); 0 (Hypoglycemic Agents); 0 (Pharmaceutical Preparations)

L62 ANSWER 24 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2003126161 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12640189
TITLE: Clinical features and metabolic derangements in acquired generalized lipodystrophy: case reports and review of the literature.
AUTHOR: Misra Anoop; Garg Abhimanyu
CORPORATE SOURCE: Division of Nutrition and Metabolic Diseases, Department of Internal Medicine, University of Texas Southwestern Medical Center at Dallas, 75390, USA.
CONTRACT NUMBER: M01-RR00633 (NCRR)
R01-DK54387 (NIDDK)

SOURCE: Medicine, (2003 Mar) Vol. 82, No. 2, pp. 129-46. Ref: 75
Journal code: 2985248R. ISSN: 0025-7974.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 18 Mar 2003
Last Updated on STN: 18 Apr 2003
Entered Medline: 17 Apr 2003

AB We present clinical descriptions, metabolic features, and patterns of body fat loss of 16 patients with acquired generalized lipodystrophy (AGL) seen by us over the last 10 years. In addition, we review 63 cases of AGL reported in the literature. Based on these data, we propose new diagnostic criteria for AGL, the essential criterion being selective loss of body fat from large regions of the body occurring after birth. We also propose a subclassification of AGL into 3 varieties, type 1, the panniculitis variety; type 2, the autoimmune disease variety; and type 3, the idiopathic variety, which affect nearly 25%, 25%, and 50% of patients, respectively. Most of the patients presented in childhood and adolescence. Females were affected approximately 3 times more than males. Subcutaneous fat loss was severe and usually affected the face, trunk, abdomen, and extremities. In some patients, fat loss also involved the palms and soles and intraabdominal region; however, the bone marrow and retroorbital fat were preserved in all patients. Clinically, patients may have voracious appetite, fatigue, and acanthosis nigricans. Hepatomegaly was common, mostly due to hepatic steatosis. Most AGL patients had fasting and/or postprandial hyperinsulinemia, diabetes mellitus, hypertriglyceridemia, and low serum levels of high-density lipoprotein cholesterol, leptin, and adiponectin. Diabetes mellitus and hypertriglyceridemia were less prevalent in the panniculitis variety compared with the idiopathic and autoimmune varieties. The management of AGL includes cosmetic surgery for loss of fat. Severe hypertriglyceridemia should be treated with a very low-fat diet and omega-3 polyunsaturated fatty acid supplementation from fish oils. Management of diabetes is difficult and may necessitate insulin therapy in large doses. Insulin sensitizers such as metformin and thiazolidinediones have been used, although their long-term efficacy and safety remain unknown. Subcutaneous administration of recombinant leptin in AGL patients with hypoleptinemia effectively improves hyperglycemia, hypertriglyceridemia, and hepatic steatosis. Leptin therapy, however, remains investigational. Fibrates alone or in combination with statins may be used to treat hypertriglyceridemia.

CT Check Tags: Female; Male
*Adipose Tissue: ME, metabolism
Adipose Tissue: RA, radiography
Adipose Tissue: SU, surgery
Adolescent
Adult
Antilipemic Agents: TU, therapeutic use
Body Composition
Child
Child, Preschool
Diabetes Complications
Diabetes Mellitus: DT, drug therapy
Glucose Intolerance: ET, etiology
Glucose Intolerance: TH, therapy
Humans

Hypertriglyceridemia: DT, drug therapy
Hypertriglyceridemia: ET, etiology
Leptin: ME, metabolism
Leptin: TU, therapeutic use
*Lipodystrophy: DI, diagnosis
*Lipodystrophy: ME, metabolism
Lipodystrophy: TH, therapy
Magnetic Resonance Imaging
Middle Aged
Reconstructive Surgical Procedures
Treatment Outcome
CN 0 (Antilipemic Agents); 0 (Leptin)

L62 ANSWER 25 OF 41 MEDLINE on STN
ACCESSION NUMBER: 2003348697 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12880692
TITLE: Reducing coronary heart disease associated with type 2 diabetes: lifestyle intervention and treatment of dyslipidaemia.
AUTHOR: Tuomilehto Jaakko
CORPORATE SOURCE: Diabetes and Genetic Epidemiology Unit, National Public Health Institute, Mannerheimintie 166, 00300 Helsinki, Finland.. jaakko.tuomilehto@ktl.fi
SOURCE: Diabetes research and clinical practice, (2003 Jul) Vol. 61 Suppl 1, pp. S27-34. Ref: 23
Journal code: 8508335. ISSN: 0168-8227.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200404
ENTRY DATE: Entered STN: 26 Jul 2003
Last Updated on STN: 24 Apr 2004
Entered Medline: 23 Apr 2004

AB Efforts to reduce the burden of coronary heart disease (CHD) associated with type 2 diabetes should include increased emphasis on preventing progression to diabetes in individuals with impaired glucose tolerance. Recent large-scale studies have shown that lifestyle intervention can reduce progression to diabetes by nearly 60%. Dyslipidaemia is a risk factor for CHD in diabetic patients. Accumulation of evidence indicating significant reductions in CHD risk with statin treatment to lower low-density lipoprotein (LDL)-cholesterol has led to the recommendation that reduction of LDL-cholesterol be considered the highest priority in treating diabetic dyslipidaemia; additional aims of treatment include raising high-density lipoprotein (HDL)-cholesterol and reducing triglyceride levels. In a recent trial of rosuvastatin alone or combined with fenofibrate in diabetic patients with combined hyperlipidaemia, rosuvastatin 40 mg monotherapy produced marked beneficial changes in LDL-cholesterol (-47%), HDL-cholesterol (+6%) and triglycerides (-30%), with the combination of lower-dose rosuvastatin (10 mg) and fenofibrate producing a significantly greater triglyceride reduction (-47%) and comparable changes in other lipid measures. Combination therapies for dyslipidaemia may be the key to optimizing CHD risk reduction in type 2 diabetes.

CT Antilipemic Agents: TU, therapeutic use
Body Weight
Clinical Trials
Coronary Disease: ET, etiology
*Coronary Disease: PC, prevention & control
Coronary Disease: TH, therapy
*Diabetes Mellitus, Type 2: CO, complications

Diabetes Mellitus, Type 2: ME, metabolism
Diabetes Mellitus, Type 2: PC, prevention & control
Drug Therapy, Combination
Fluorobenzenes: TU, therapeutic use
Humans
Hyperlipidemias: CO, complications
*Hyperlipidemias: TH, therapy
Hypoglycemic Agents: TU, therapeutic use
Life Style
Metformin: TU, therapeutic use
Motor Activity
Procetofen: TU, therapeutic use
Pyrimidines: TU, therapeutic use
Sulfonamides: TU, therapeutic use
RN 287714-41-4 (rosuvastatin); 49562-28-9 (Procetofen); 657-24-9 (Metformin)
CN 0 (Antilipemic Agents); 0 (Fluorobenzenes); 0 (Hypoglycemic Agents); 0 (Pyrimidines); 0 (Sulfonamides)

L62 ANSWER 26 OF 41 MEDLINE on STN
ACCESSION NUMBER: 1999051815 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9834750
TITLE: Care of adults with type 2 diabetes mellitus. A review of the evidence.
AUTHOR: O'Connor P J; Spann S J; Woolf S H
CORPORATE SOURCE: HealthPartners Research Foundation, Minneapolis, Minnesota 55440-1309, USA.
SOURCE: The Journal of family practice, (1998 Nov) Vol. 47, No. 5 Suppl, pp. S13-22. Ref: 67
Journal code: 7502590. ISSN: 0094-3509.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 15 Jan 1999
Last Updated on STN: 15 Jan 1999
Entered Medline: 16 Dec 1998

AB BACKGROUND: The purpose of this study was to provide primary care physicians with a concise review of the evidence that guides selected aspects of type 2 diabetes care, including glycemic control, macrovascular risk reduction, and screening for microvascular complications of diabetes. METHODS: We identified randomized clinical trials that addressed selected aspects of the care of adults with type 2 diabetes using systematic literature review, review of existing clinical guidelines, and other sources. The results of these trials were interpreted as absolute risk reduction, and the number of patients that need to be treated to obtain a specific clinical outcome was calculated. RESULTS: Good glycemic control with metformin may reduce overall mortality in obese patients with type 2 diabetes (number need to treat [NNT] = 14 for 10 years), and improved blood pressure control reduced diabetes-related mortality (NNT = 15 for 10 years); improved glycemic control with agents other than metformin, or with combinations including metformin, does not reduce diabetes-related or overall mortality. Major cardiovascular events (CVE) in type 2 diabetes can be prevented by control of blood pressure with low-dose diuretics, atenolol, or angiotensin-converting enzyme inhibitors (NNT = 10 to 20 for 5 to 10 years for primary prevention of one CVE); by use of aspirin (NNT = 45 for 5 years for primary prevention of one CVE); and by use of simvastatin to lower low-density lipoprotein (LDL) cholesterol (NNT = 6 for 5 years for secondary prevention of one CVE). Glycemic control (NNT = 19 for 10

years) and hypertension control (NNT = 6 for 10 years) slow the progression of complications in patients with type 2 diabetes. Retinopathy and nephropathy are more preventable than neuropathy. The benefits of glycemic control are less for patients with shorter life expectancy and are greater for those with the highest levels of Hb A1c because larger Hb A1c improvements can be achieved in such patients. Periodic screening of patients for eye, kidney, and foot complications is supported because effective early treatment of these complications is available. CONCLUSIONS: In patients with type 2 diabetes, control of hypertension reduces microvascular and macrovascular complications more than glycemic control does. Control of LDL cholesterol with statins, aspirin, and smoking cessation reduce major cardiovascular events. Metformin reduces overall mortality in obese patients with creatinine levels < 1.5 mg/dL. Glycemic control reduces microvascular complications. The evidence supports angiotensin-converting enzyme inhibitors, atenolol, or low-dose diuretics for blood pressure control. Effective treatment of eye, kidney, and foot complications is available, and regular screening for these complications is justified.

CT Adult
Aged
Diabetes Mellitus, Type 2: CO, complications
Diabetes Mellitus, Type 2: MO, mortality
*Diabetes Mellitus, Type 2: TH, therapy
Diabetic Nephropathies: PC, prevention & control
Diabetic Neuropathies: PC, prevention & control
Evidence-Based Medicine
Humans
Hypertension: CO, complications
Hypertension: DT, drug therapy
Hypertension: PC, prevention & control
Middle Aged
Randomized Controlled Trials

L62 ANSWER 27 OF 41 EMBASE

ACCESSION NUMBER: 2002182153 EMBASE Full-text
TITLE: Teaching patients to monitor their risk factors retards the progression of vascular complications in high-risk patients with Type 2 diabetes mellitus
- A randomized prospective study.
AUTHOR: Rachmani R.; Levi Z.; Slavachevski I.; Avin M.; Ravid M.
CORPORATE SOURCE: Prof. M. Ravid, Meir Hospital, Kfar-Sava 44281, Israel. motirv@clalit.org.il
SOURCE: Diabetic Medicine, (2002) Vol. 19, No. 5, pp. 385-392.
Refs: 38
ISSN: 0742-3071 CODEN: DIMEEV
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
017 Public Health, Social Medicine and Epidemiology
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 6 Jun 2002
Last Updated on STN: 6 Jun 2002

AB Aims: Intensive management of risk parameters in diabetic patients may retard the progression of both micro- and macrovascular complications. Intensified care requires expert staff and is expensive. The aim of the present study was to examine whether sharing the therapeutic responsibility with the patients will improve the outcome. Methods: A randomized prospective study of 165

patients with diabetes mellitus Type 2, hypertension (>140/90 mmHg) and hyperlipidaemia (LDL-C >120 mg/dl). Patients were randomly allocated to standard annual consultation (SC) or to a patient participation programme (PP). The medical care for both groups was administered by primary care physicians, who were unaware of the nature of the intervention. Results: At 4 years the mean blood pressure was 148/88 (±6.1/1.7) mmHg in the SC patients vs. 142/84 (±5.8/1.8) mmHg in the PP group (P=0.02). The mean LDL-C was 124±8 and 114±6 mg/dl (P=0.01) and the mean HbA(1c) was 8.9±1.2% and 8.2±1.5% (P=0.04) in the SC and PP groups, respectively. The average annual fall in estimated glomerular filtration rate was 3.5 ml/min per year in the SC group vs. 2.25 in the PP group (P<0.05). Albumin/creatinine ratio >300 mg/g developed in four SC patients vs. none of the PP patients. There was a total of 36 cardiovascular events in the SC group vs. 23 in the PP group (P=0.04). All patients in the PP group received ACE inhibitors (or AII blockers) and statins vs. 52% and 43%, respectively, in the SC group. Glucose-lowering regimens were similar. Conclusions: Well-informed and motivated patients were more insistent to reach and maintain target values of the main risk factors of diabetic complications. The differences between the PP and SC groups were of the same order of magnitude as those between intensive and standard care groups in other studies albeit with, comparatively, a very modest cost.

CT Medical Descriptors:
*non insulin dependent diabetes mellitus: DT, drug therapy
*patient education
*diabetic angiopathy: CO, complication
*diabetic angiopathy: PC, prevention
risk factor
hypertension: DT, drug therapy
hyperlipidemia: DT, drug therapy
medical care
physician
blood pressure
glomerulus filtration rate
microalbuminuria
treatment outcome
cardiovascular risk
disease course
high risk population
human
male
female
major clinical study
clinical trial
randomized controlled trial
controlled study
aged
adult
article
Drug Descriptors:
*low density lipoprotein cholesterol: EC, endogenous compound
*hemoglobin A1c: EC, endogenous compound
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: PD, pharmacology
beta adrenergic receptor blocking agent: DT, drug therapy
beta adrenergic receptor blocking agent: PD, pharmacology
alpha adrenergic receptor blocking agent: DT, drug therapy
alpha adrenergic receptor blocking agent: PD, pharmacology
antilipemic agent: DT, drug therapy
antilipemic agent: PD, pharmacology
hydrochlorothiazide: DT, drug therapy
hydrochlorothiazide: PD, pharmacology

acetylsalicylic acid: DT, drug therapy
sulfonylurea: DT, drug therapy
sulfonylurea: PD, pharmacology
metformin: DT, drug therapy
metformin: PD, pharmacology
insulin: DT, drug therapy
insulin: PD, pharmacology
calcium channel blocking agent: DT, drug therapy
calcium channel blocking agent: PD, pharmacology
glucose: EC, endogenous compound
RN (hemoglobin A1c) 62572-11-6; (hydrochlorothiazide) 58-93-5; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (metformin) 1115-70-4, 657-24-9; (insulin) 9004-10-8; (glucose) 50-99-7, 84778-64-3
CN Aspirin

L62 ANSWER 28 OF 41 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2002221449 EMBASE Full-text
TITLE: Lipid response to pioglitazone in diabetic patients: Clinical observations from a retrospective chart review.
AUTHOR: King A.B.; Armstrong D.U.
CORPORATE SOURCE: Dr. A.B. King, Diabetes Care Center, 1119 Pajaro St., Salinas, CA 93901, United States. akvineyards@email.msn.com
SOURCE: Diabetes Technology and Therapeutics, (2002) Vol. 4, No. 2, pp. 145-151. .
Refs: 19
ISSN: 1520-9156 CODEN: DTTHFH
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 11 Jul 2002
Last Updated on STN: 11 Jul 2002

AB The objective of this study was to determine whether improvements in the lipid profile observed in controlled clinical trials with pioglitazone are seen in the clinical practice setting, and to ascertain the influence of concurrent statin treatment. Charts of 100 consecutive patients with type 2 diabetes (mean age 56.8 years) treated with pioglitazone (45 mg/day) for 2-4 months were retrospectively analyzed for changes in serum lipids, glycemic parameters, and body weight. Subanalyses were performed on the relationship of lipid changes to baseline lipid values and to concurrent statin therapy. Pioglitazone was associated with statistically significant ($p < 0.001$) changes from baseline in HbAlc (mean decrease 1.09%), body weight (mean increase 1.76 kg), HDL cholesterol (HDL-C) levels (mean increase 15.6%), and triglycerides (mean decrease 9.9%). There was an increase (+1.09%) in mean individual LDL-C levels from baseline values, but this change was not statistically significant. The greatest absolute and percentage improvements in HDL-C and triglycerides were observed in patients who had the greatest lipid abnormalities at baseline: in patients with baseline HDL-C < 35 mg/dL, mean individual HDL-C values increased by 31% ($p < 0.001$); in those with baseline triglycerides > 399 mg/dL, triglyceride levels decreased by 46% ($p < 0.001$); and in patients with baseline LDL-C > 129 mg/dL, mean individual LDL-C values decreased by 10.6% ($p < 0.001$). Subgroup analysis showed similar beneficial changes in HDL-C and triglycerides in patients who were not receiving concurrent statin therapy (n = 48) as in those who were receiving statins (n = 49). This observational study demonstrated that significant improvements in

HDL-C and triglyceride levels can be achieved with pioglitazone in the clinical practice setting. The greatest improvements occurred in patients with the worst baseline lipid levels, and benefits were seen regardless of whether patients were receiving concurrent statin therapy.

CT Medical Descriptors:
*diabetes mellitus: DT, drug therapy
*dyslipidemia: DT, drug therapy
drug response
cholesterol blood level
triacylglycerol blood level
drug effect
edema: SI, side effect
hypoglycemia: SI, side effect
anemia: SI, side effect
human
male
female
clinical trial
aged
adult
article
priority journal
Drug Descriptors:
*pioglitazone: AE, adverse drug reaction
*pioglitazone: CT, clinical trial
*pioglitazone: CB, drug combination
*pioglitazone: DT, drug therapy
*pioglitazone: PD, pharmacology
*lipid
hydroxymethylglutaryl coenzyme A reductase inhibitor: CB, drug combination
hydroxymethylglutaryl coenzyme A reductase inhibitor: DT, drug therapy
high density lipoprotein cholesterol
triacylglycerol
metformin: DT, drug therapy
sulfonylurea derivative: DT, drug therapy
repaglinide: DT, drug therapy
insulin: DT, drug therapy
hemoglobin A1c
RN (pioglitazone) 105355-27-9, 111025-46-8; (lipid) 66455-18-3; (metformin) 1115-70-4, 657-24-9; (repaglinide) 135062-02-1; (insulin) 9004-10-8; (hemoglobin A1c) 62572-11-6

L62 ANSWER 29 OF 41 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2001123661 EMBASE Full-text
TITLE: Simvastatin treatment on postprandial hypertriglyceridemia in type 2 diabetes mellitus
patients with combined hyperlipidemia.
AUTHOR: Sheu W.H.-H.; Jeng C.-Y.; Lee W.-J.; Lin S.-Y.; Pei D.; Chen Y.-T.
CORPORATE SOURCE: Dr. W.H.-H. Sheu, Div. of Endocrinology and Metabolism, Taichung Veterans General Hospital, No. 160, Section 3, Chung-Kang Road, Taichung 407, Taiwan,Province of China
SOURCE: Metabolism: Clinical and Experimental, (2001) Vol. 50, No. 3, pp. 355-359. .
Refs: 40
ISSN: 0026-0495 CODEN: METAAJ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 029 Clinical Biochemistry
030 Pharmacology
003 Endocrinology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 12 Apr 2001
Last Updated on STN: 12 Apr 2001

AB Recent studies have shown that statins are effective in reducing fasting low-density lipoprotein-cholesterol (LDL-C) and triglyceride levels. However, it remains unknown if treatment with statins also lowers daily postprandial triglyceride concentrations, which may promote atherogenesis in type 2 diabetes subjects. Forty-one subjects with type 2 diabetes and combined hyperlipidemia who had stable glycemic control were randomly assigned to take simvastatin 20 mg (n = 27) or a placebo (n = 14) once daily for 12 weeks. The medication dosage was doubled after 4 weeks if a subject's LDL-C was not less than 130 mg/dL. Among these participants, 24 subjects (15 on simvastatin and 9 on placebo) agreed to take a meal tolerance test with isocaloric mixed meals (carbohydrate, 52%; fat, 33%, and protein, 15% of the daily caloric intake) and daytime hourly blood sampling from 8 AM to 4 PM. Simvastatin treatment reduced the fasting total cholesterol level from 237 ± 5 to 178 ± 6 mg/dL (-25%), the LDL cholesterol level from 150 ± 6 to 87 ± 5 mg/dL (-40%), and raised high-density lipoprotein-cholesterol (HDL-C) level from 36 ± 2 to 40 ± 2 mg/dL (+11%) (all P < .001). Fasting and daily ambient triglyceride concentrations from 8 AM to 4 PM decreased significantly in response to simvastatin administration (P < .001), but not to the placebo (P = .305). Simvastatin treatment not only decreased total cholesterol and LDL-C levels and increased HDL-C levels effectively, it also decreased fasting, as well as daily postprandial triglyceride concentrations, but had no effect on glycemic control in type 2 diabetes subjects with combined hyperlipidemia. Copyright .COPYRGT. 2001 by W.B. Saunders Company.

CT Medical Descriptors:
*hypertriglyceridemia: DT, drug therapy
*hypertriglyceridemia: DM, disease management
*non insulin dependent diabetes mellitus: DT, drug therapy
*non insulin dependent diabetes mellitus: DM, disease management
*hyperlipidemia: DT, drug therapy
*hyperlipidemia: DM, disease management
controlled study
human
clinical article
clinical trial
randomized controlled trial
double blind procedure
female
male
adult
drug efficacy
postprandial state
triacylglycerol blood level
cholesterol blood level
diabetes control
atherogenesis
dose response
test meal
disease association
caloric intake
nutritional tolerance
blood sampling
diet restriction

comparative study
drug potency
drug use
body mass
treatment outcome
article
priority journal
Drug Descriptors:
*simvastatin: PD, pharmacology
*simvastatin: CT, clinical trial
*simvastatin: DO, drug dose
*simvastatin: DT, drug therapy
placebo
triacylglycerol: EC, endogenous compound
low density lipoprotein cholesterol: EC, endogenous compound
carbohydrate
protein
fat
high density lipoprotein cholesterol: EC, endogenous compound
antidiabetic agent: DT, drug therapy
antidiabetic agent: PO, oral drug administration
antidiabetic agent: PD, pharmacology
antihypertensive agent: DT, drug therapy
sulfonylurea: DT, drug therapy
metformin: DT, drug therapy
glucose: EC, endogenous compound
RN (simvastatin) 79902-63-9; (protein) 67254-75-5; (metformin) 1115-70-4, 657-24-9; (glucose) 50-99-7, 84778-64-3

L62 ANSWER 30 OF 41 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2001387086 EMBASE Full-text
TITLE: Highlights from the 61st Scientific Sessions of the ADA June 22-26, 2001, Philadelphia, USA.
SOURCE: Practical Diabetes International, (2001) Vol. 18, No. 7, pp. 251-258.
ISSN: 1357-8170 CODEN: PDINFY
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 003 Endocrinology
017 Public Health, Social Medicine and Epidemiology
030 Pharmacology
029 Clinical Biochemistry
039 Pharmacy
038 Adverse Reactions Titles
006 Internal Medicine
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Nov 2001
Last Updated on STN: 26 Nov 2001
CT Medical Descriptors:
*diabetes mellitus: DT, drug therapy
*diabetes mellitus: SU, surgery
*diabetes mellitus: DM, disease management
*diabetes mellitus: EP, epidemiology
*diabetes mellitus: PC, prevention
human
clinical trial
nonhuman
symposium

socioeconomics
risk assessment
physician attitude
United States
education
age
high risk population
prevalence
dose response
elderly care
health survey
lifestyle
postprandial state
  hyperglycemia: CO, complication
  hyperglycemia: PC, prevention
  hyperglycemia: DT, drug therapy
diabetic obesity
disease association
diet
health promotion
weight reduction
Internet
cardiovascular disease: PC, prevention
pancreas islet transplantation
immunosuppressive treatment
long term care
blood glucose monitoring
awareness
social aspect
diabetes control
health care quality
bleeding: CO, complication
portal vein thrombosis: CO, complication
bladder injury: CO, complication
hypercholesterolemia: SI, side effect
metabolic disorder: SI, side effect
United Kingdom
evidence based medicine
quality of life
drug delivery system
drug absorption
visual impairment
drug mechanism
conference paper
CT Drug Descriptors:
*antidiabetic agent: DT, drug therapy
  *antidiabetic agent: CB, drug combination
*antidiabetic agent: DV, drug development
*antidiabetic agent: PR, pharmaceutics
*antidiabetic agent: CT, clinical trial
*antidiabetic agent: IH, inhalational drug administration
*antidiabetic agent: AE, adverse drug reaction
*antidiabetic agent: PO, oral drug administration
*antidiabetic agent: DO, drug dose
*antidiabetic agent: PK, pharmacokinetics
*antidiabetic agent: PD, pharmacology
*antidiabetic agent: SC, subcutaneous drug administration
insulin: DT, drug therapy
  insulin: CB, drug combination
insulin: PR, pharmaceutics

insulin: CT, clinical trial
insulin: IH, inhalational drug administration
insulin: CM, drug comparison
insulin: AE, adverse drug reaction
insulin: PO, oral drug administration
insulin: DO, drug dose
insulin: PK, pharmacokinetics
repaglinide: DT, drug therapy
repaglinide: PD, pharmacology
repaglinide: CT, clinical trial
repaglinide: DO, drug dose
nateglinide: DT, drug therapy
nateglinide: PD, pharmacology
nateglinide: CT, clinical trial
nateglinide: CM, drug comparison
tetrahydrolipstatin: DT, drug therapy
  statin
immunosuppressive agent: DT, drug therapy
  immunosuppressive agent: CB, drug combination
immunosuppressive agent: AE, adverse drug reaction
immunosuppressive agent: DO, drug dose
glucose: EC, endogenous compound
rapamycin: DT, drug therapy
  rapamycin: CB, drug combination
rapamycin: AE, adverse drug reaction
rapamycin: DO, drug dose
rapamycin: CT, clinical trial
rapamycin: PD, pharmacology
tsukubaenolide: DT, drug therapy
  tsukubaenolide: CB, drug combination
tsukubaenolide: AE, adverse drug reaction
thiazole derivative: DV, drug development
thiazole derivative: DT, drug therapy
  thiazole derivative: CB, drug combination
thiazole derivative: PD, pharmacology
glimepiride: DV, drug development
glimepiride: DT, drug therapy
  glimepiride: CB, drug combination
troglitazone: DV, drug development
troglitazone: DT, drug therapy
  troglitazone: CB, drug combination
insulin derivative: DT, drug therapy
insulin derivative: CT, clinical trial
  insulin derivative: CB, drug combination
isophane insulin: DT, drug therapy
  isophane insulin: CB, drug combination
isophane insulin: CT, clinical trial
isophane insulin: SC, subcutaneous drug administration
isophane insulin: AE, adverse drug reaction
sulfonylurea: DT, drug therapy
sulfonylurea: PD, pharmacology
  metformin: DT, drug therapy
  metformin: PD, pharmacology
  metformin: CM, drug comparison
placebo
atorvastatin: DT, drug therapy
atorvastatin: CT, clinical trial
atorvastatin: DO, drug dose
rosuvastatin: DT, drug therapy
unclassified drug

RN (insulin) 9004-10-8; (repaglinide) 135062-02-1; (nateglinide) 105746-37-0, 105816-04-4, 105816-06-6; (tetrahydrolipstatin) 96829-58-2; (glucose) 50-99-7, 84778-64-3; (rapamycin) 53123-88-9; (tsukubaenolide) 104987-11-3; (glimepiride) 93479-97-1; (troglitazone) 97322-87-7; (isophane insulin) 9004-17-5; (metformin) 1115-70-4, 657-24-9; (atorvastatin) 134523-00-5, 134523-03-8
CN Orlistat

L62 ANSWER 31 OF 41 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2001304504 EMBASE Full-text
TITLE: Heart disease in Asian people with diabetes.
AUTHOR: Lawrence I.G.; McNally P.G.
CORPORATE SOURCE: Dr. I.G. Lawrence, Dept. of Diabetes and Endocrinology, Leicester Royal Infirmary, Univ. Hosp. of Leicester NHS Trust, Infirmary Square, Leicester LE1 5WW, United Kingdom
SOURCE: Practical Diabetes International, (2001) Vol. 18, No. 6, pp. 192-196. .
Refs: 36
ISSN: 1357-8170 CODEN: PDINFY
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
003 Endocrinology
017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index
030 Pharmacology
029 Clinical Biochemistry
036 Health Policy, Economics and Management
005 General Pathology and Pathological Anatomy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Sep 2001
Last Updated on STN: 13 Sep 2001

AB Type 2 diabetes is increased up to four-fold in middle-aged and older Indo-Asian people, and associated with increased coronary heart disease (CHD), and premature morbidity and mortality. Seventy-seven percent of deaths in Indo-Asian people with diabetes were caused by cardiovascular disease, compared with 46% European deaths, in the Southall Diabetes Survey. The Indo-Asian communities have an increased inherited lipoprotein (a) level compared to white Europeans, whilst migration results in the unmasking of a cluster of cardiovascular risk factors incorporating central obesity, hyperinsulinaemia, type 2 diabetes and dyslipidaemia. Conventional cardiovascular risk factors are important, and in India, current smoking, hypertension and overt diabetes mellitus are the strongest predictors of a first acute myocardial infarction (AMI). Hyperlipidaemia may have a less important causal role in an Indian setting, but the situation is likely to be different in a migratory Indo-Asian population. Unfortunately there is a lamentable lack of intervention studies in Indo-Asian diabetic people with CHD, and currently the evidence base from other populations needs to be extrapolated. The six month mortality in Indo-Asian people post AMI is double the white European population, despite similar use of aspirin, thrombolysis and beta blockade, and is primarily due to the increased prevalence of diabetes. This stresses the importance of active treatment of all cardiovascular risk factors, including hyperglycaemia in the peri-infarct period. Active health promotion addressing physical activity and modifying dietary intake is crucial in the Indo-Asian communities, and campaigns such as Project Dil in Leicestershire have incorporated both primary and secondary prevention. The extrapolated evidence base would suggest that early use of angiotensin-converting enzyme inhibition, statin and/or fibrate therapy, and insulin therapy may all benefit Indo-Asian diabetic people with

CHD, while metformin should be the first-line oral hypoglycaemic agent in most Indo-Asian diabetic people without CHD. Copyright .COPYRGT. 2001 John Wiley & Sons, Ltd.

CT Medical Descriptors:
*ischemic heart disease: ET, etiology
*ischemic heart disease: EP, epidemiology
*ischemic heart disease: DT, drug therapy
*ischemic heart disease: DM, disease management
*ischemic heart disease: TH, therapy
*ischemic heart disease: PC, prevention
*non insulin dependent diabetes mellitus: DT, drug therapy
*non insulin dependent diabetes mellitus: DM, disease management
*non insulin dependent diabetes mellitus: TH, therapy
*non insulin dependent diabetes mellitus: PC, prevention
human
clinical trial
Asian
disease association
morbidity
mortality
cardiovascular disease
Europe
health survey
lipoprotein blood level
migration
cardiovascular risk
obesity
hyperinsulinemia
dyslipidemia
India
smoking
hypertension
acute heart infarction
hyperlipidemia
evidence based medicine
population research
hyperglycemia
prevalence
health promotion
physical activity
dietary intake
primary prevention
secondary prevention
blood clot lysis
beta adrenergic receptor blocking
pathogenesis
health care delivery
treatment outcome
risk factor
disease marker
review
Drug Descriptors:
lipoprotein: EC, endogenous compound
acetylsalicylic acid: DT, drug therapy
fibrinolytic agent: DT, drug therapy
beta adrenergic receptor blocking agent: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
antilipemic agent: DT, drug therapy
fibric acid derivative: DT, drug therapy
insulin: DT, drug therapy

insulin: CB, drug combination
metformin: DT, drug therapy
metformin: PO, oral drug administration
oral antidiabetic agent: DT, drug therapy
oral antidiabetic agent: PO, oral drug administration
gemfibrozil: DT, drug therapy
thiazole derivative: DT, drug therapy
thiazole derivative: CT, clinical trial
thiazole derivative: PD, pharmacology
rosiglitazone: DT, drug therapy
rosiglitazone: CT, clinical trial
rosiglitazone: PD, pharmacology
pioglitazone: DT, drug therapy
glucose: CB, drug combination
glucose: DT, drug therapy
potassium: CB, drug combination
potassium: DT, drug therapy
RN (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (insulin) 9004-10-8; (metformin) 1115-70-4, 657-24-9; (gemfibrozil) 25812-30-0; (rosiglitazone) 122320-73-4, 155141-29-0; (pioglitazone) 105355-27-9, 111025-46-8; (glucose) 50-99-7, 84778-64-3; (potassium) 7440-09-7

L62 ANSWER 32 OF 41 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2001084431 EMBASE Full-text
TITLE: Management of type 2 diabetes mellitus in the elderly: Special considerations.
AUTHOR: Rosenstock J.
CORPORATE SOURCE: Dr. J. Rosenstock, Dallas Diabetes and Endocrine Center, Medical City Dallas, 7777 Forest Lane, Dallas, TX 75230, United States. juliorosenstock@dallasdiabetes.com
SOURCE: Drugs and Aging, (2001) Vol. 18, No. 1, pp. 31-44.
Refs: 52
ISSN: 1170-229X CODEN: DRAGE6
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
020 Gerontology and Geriatrics
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 Mar 2001
Last Updated on STN: 29 Mar 2001

AB The principles of managing type 2 diabetes mellitus in the elderly are no different from those in younger patients but the priorities and therapeutic strategies need to be cautiously individualised. The objectives of treatment are to improve glycaemic control in a stepwise approach that involves nonpharmacological methods including diet and exercise, and pharmacological therapy including mixtures of oral antihyperglycaemic agents alone or in combination with insulin. Although the goals of treatment may be the same for elderly and younger patients, certain aspects of type 2 diabetes in the elderly require special consideration. Treatment decisions are influenced by age and life expectancy comorbid conditions and severity of the vascular complications. Adherence to dietary therapy, physical activity, and medication regimens may be compromised by comorbid conditions and psychosocial limitations. Drug-induced hypoglycaemia has been the main consideration and the most serious potential complication. In addition, the long term macrovascular and microvascular complications of type 2 diabetes are a source

of significant morbidity and mortality. Indeed, vascular and neuropathic complications are already present at the time of diagnosis in a significant number of patients, and the impact of improved diabetes control depends on the age and life expectancy of the patient. Age-related changes in pharmacokinetics and the potential for adverse effects and drug interactions should also be considered when choosing appropriate pharmacological therapy. In general, a conservative and stepwise approach to the treatment of the elderly patient with type 2 diabetes is suggested: treatment may be initiated with monotherapy, followed by early intervention with a combination of oral agents including a sulphonylurea as a foundation insulin secretagogue in addition to a supplemental insulin sensitiser. Insulin therapy is eventually required if significant hyperglycaemia [glycosylated haemoglobin (HbA (1c)) >8%] persists despite oral combination therapy. Combination therapy with evening insulin and a long-acting sulphonylurea such as glimepiride is an effective strategy to improve hyperglycaemia in the elderly patient with type 2 diabetes in whom polypharmacy with oral agents is unsuccessful. In addition, such a regimen is simple to follow for the patient who may not be able to adhere to a more complicated insulin regimen. Hyperglycaemia in the elderly can be managed well with practical intervention and a straightforward treatment plan to enhance compliance. Optimal glycaemic control should be possible for every patient if treatment is individualised: however, strict glycaemic control may not be achievable in all patients or even desirable in many elderly patients.

CT Medical Descriptors:
*non insulin dependent diabetes mellitus: DT, drug therapy
treatment planning
exercise
age
life expectancy
disease severity
diet therapy
hypoglycemia: SI, side effect
mortality
morbidity
clinical feature
coronary artery disease: CO, complication
cerebrovascular disease: CO, complication
peripheral vascular disease: CO, complication
hyperlipidemia: CO, complication
hyperlipidemia: DT, drug therapy
diabetic nephropathy: CO, complication
diabetic nephropathy: DT, drug therapy
diabetic neuropathy: CO, complication
diabetic neuropathy: DT, drug therapy
stomach paresis: CO, complication
side effect: SI, side effect
practice guideline
human
aged
review
priority journal
Drug Descriptors:
*antidiabetic agent: AE, adverse drug reaction
*antidiabetic agent: CB, drug combination
*antidiabetic agent: DT, drug therapy
*insulin: CB, drug combination
*insulin: DT, drug therapy
sulfonylurea derivative: CB, drug combination
sulfonylurea derivative: DT, drug therapy
hemoglobin A1c: EC, endogenous compound

glimepiride: CB, drug combination
glimepiride: DT, drug therapy
biguanide: DT, drug therapy
thiazole derivative: AE, adverse drug reaction
thiazole derivative: CB, drug combination
thiazole derivative: DT, drug therapy
thiazole derivative: PO, oral drug administration
meglitinide: AE, adverse drug reaction
meglitinide: CB, drug combination
meglitinide: DT, drug therapy
meglitinide: PK, pharmacokinetics
alpha glucosidase inhibitor: AE, adverse drug reaction
alpha glucosidase inhibitor: DT, drug therapy
alpha glucosidase inhibitor: PK, pharmacokinetics
statin: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
ramipril: DT, drug therapy
metformin: AE, adverse drug reaction
metformin: CB, drug combination
metformin: DT, drug therapy
metformin: PK, pharmacokinetics
metformin: PO, oral drug administration
acarbose: AE, adverse drug reaction
acarbose: CB, drug combination
acarbose: DT, drug therapy
acarbose: PK, pharmacokinetics
pioglitazone: AE, adverse drug reaction
pioglitazone: CB, drug combination
pioglitazone: DT, drug therapy
pioglitazone: PO, oral drug administration
rosiglitazone: AE, adverse drug reaction
rosiglitazone: CB, drug combination
rosiglitazone: DT, drug therapy
rosiglitazone: PO, oral drug administration
glibenclamide: DT, drug therapy
glipizide: DT, drug therapy
troglitazone: AE, adverse drug reaction
troglitazone: DT, drug therapy
troglitazone: PO, oral drug administration
repaglinide: AE, adverse drug reaction
repaglinide: AD, drug administration
repaglinide: CB, drug combination
repaglinide: PK, pharmacokinetics
miglitol: DT, drug therapy

RN (insulin) 9004-10-8; (hemoglobin A1c) 62572-11-6; (glimepiride) 93479-97-1; (biguanide) 56-03-1; (meglitinide) 54870-28-9; (ramipril) 87333-19-5; (metformin) 1115-70-4, 657-24-9; (acarbose) 56180-94-0; (pioglitazone) 105355-27-9, 111025-46-8; (rosiglitazone) 122320-73-4, 155141-29-0; (glibenclamide) 10238-21-8; (glipizide) 29094-61-9; (troglitazone) 97322-87-7; (repaglinide) 135062-02-1; (miglitol) 72432-03-2

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ACCESSION NUMBER: 2001017511 EMBASE Full-text
TITLE: Glitazones and the potential improvement of lipid profiles in diabetes patients at high risk for cardiovascular disease.
AUTHOR: Nass C.M.; Blumenthal R.S.
CORPORATE SOURCE: Dr. R.S. Blumenthal, Ciccarone Prev. Cardiology Center,

Johns Hopkins Hospital, 600 Noerth Wolfe Street, Baltimore, MD 21205, United States. rblument@jhmi.edu

SOURCE: American Journal of Managed Care, (2000) Vol. 6, No. 24 SUPPL., pp. S1247-S1256. .
Refs: 66
ISSN: 1088-0224 CODEN: AJMCFY
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
003 Endocrinology
018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
030 Pharmacology
036 Health Policy, Economics and Management
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 25 Jan 2001
Last Updated on STN: 25 Jan 2001

AB Most deaths and hospitalizations in patients with diabetes are related to atherosclerotic vascular disease. An asymptomatic patient with type 2 diabetes has a cardiovascular risk comparable to that of a patient without diabetes who has a history of a myocardial infarction. The American Heart Association classifies diabetes as a coronary heart disease risk equivalent. Thus, it is important in patients with diabetes to aim for systolic blood pressures less than 130 mm Hg, using an angiotensin-converting enzyme inhibitor-based regimen. The target hemoglobin A(1C) (HbA(1C)) for those patients is < 7%. New oral insulin-sensitizing medications, known as thiazolidinediones or glitazones, are useful to improve glycemic control. Most patients with diabetes require 2 or more oral agents to achieve optimal glucose control. Glitazones generally lower HbA(1C) by 1% to 2%. They also raise high-density lipoprotein cholesterol levels and lower triglycerides. Thus, they may potentially improve low-density lipoprotein (LDL) particle sizes by converting small, dense LDL particles into larger, less atherogenic ones. Current data concerning the lipid effects of pioglitazone and rosiglitazone are reviewed in this article.

CT Medical Descriptors:
*non insulin dependent diabetes mellitus: DT, drug therapy
*non insulin dependent diabetes mellitus: DM, disease management
*non insulin dependent diabetes mellitus: ET, etiology
*cardiovascular risk
human
case report
clinical trial
adult
female
high risk patient
drug effect
drug cost
hyperglycemia
risk assessment
glucose metabolism
insulin blood level
glucose blood level
hypoglycemia: SI, side effect
dose response
liver injury: SI, side effect
anemia: SI, side effect
weight gain
ovulation induction

dyslipidemia: DT, drug therapy
hypertension: DT, drug therapy
article
priority journal
Drug Descriptors:
*pioglitazone: PD, pharmacology
*pioglitazone: DT, drug therapy
*pioglitazone: PE, pharmacoeconomics
*pioglitazone: IT, drug interaction
*pioglitazone: CM, drug comparison
*pioglitazone: AE, adverse drug reaction
*pioglitazone: CT, clinical trial
*pioglitazone: DO, drug dose
*rosiglitazone: PD, pharmacology
*rosiglitazone: DT, drug therapy
*rosiglitazone: PE, pharmacoeconomics
*rosiglitazone: IT, drug interaction
*rosiglitazone: CM, drug comparison
*rosiglitazone: AE, adverse drug reaction
*rosiglitazone: CT, clinical trial
*rosiglitazone: CB, drug combination
*rosiglitazone: DO, drug dose
lipid: EC, endogenous compound
hemoglobin A1c: EC, endogenous compound
glucose: EC, endogenous compound
high density lipoprotein cholesterol: EC, endogenous compound
triacylglycerol: EC, endogenous compound
low density lipoprotein: EC, endogenous compound
metformin: DT, drug therapy
metformin: PD, pharmacology
metformin: PE, pharmacoeconomics
metformin: CM, drug comparison
glibenclamide: DT, drug therapy
glibenclamide: PE, pharmacoeconomics
glibenclamide: PD, pharmacology
glibenclamide: CM, drug comparison
simvastatin: DT, drug therapy
ramipril: DT, drug therapy
atenolol: DT, drug therapy
acetylsalicylic acid: DT, drug therapy
peroxisome proliferator activated receptor: EC, endogenous compound
insulin: EC, endogenous compound
troglitazone: CT, clinical trial
troglitazone: DT, drug therapy
troglitazone: PD, pharmacology
troglitazone: DO, drug dose
sulfonylurea: DT, drug therapy
sulfonylurea: CB, drug combination
sulfonylurea: DO, drug dose
sulfonylurea: CT, clinical trial
statin: DT, drug therapy
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy
RN (pioglitazone) 105355-27-9, 111025-46-8; (rosiglitazone) 122320-73-4, 155141-29-0; (lipid) 66455-18-3; (hemoglobin A1c) 62572-11-6; (glucose) 50-99-7, 84778-64-3; (metformin) 1115-70-4, 657-24-9; (glibenclamide) 10238-21-8; (simvastatin) 79902-63-9; (ramipril) 87333-19-5; (atenolol) 29122-68-7; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (insulin) 9004-10-8; (troglitazone) 97322-87-7

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ACCESSION NUMBER: 2000020275 EMBASE Full-text
TITLE: Efficacy and safety of cerivastatin for type 2 diabetes and hypercholesterolaemia.
AUTHOR: Rubinstein A.; Maritz F.J.; Soule S.G.; Markel A.; Chajek-Shaul T.; Maislos M.; Tal S.; Stolero D.
CORPORATE SOURCE: Prof. A. Rubinstein, Metabolic Unit, Tel-Aviv Sourasky Medical Centre, 6 Weisman Street, Tel-Aviv 64239, Israel
SOURCE: Journal of Cardiovascular Risk, (1999) Vol. 6, No. 6, pp. 399-403. .
Refs: 19
ISSN: 1350-6277 CODEN: JCRIEO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Jan 2000
Last Updated on STN: 20 Jan 2000

AB Background: The prevalence of coronary heart disease (CHD) is markedly increased in diabetic patients compared with nondiabetic individuals, and its prognosis is less good. Serum total and low-density lipoprotein (LDL) cholesterol concentrations have been shown to be powerful predictors of CHD morbidity and mortality in patients with type 2 diabetes. The available data suggest that the target cholesterol concentration in patients with diabetes should be similar to that in non-diabetic individuals with a previous myocardial infarction. This led us to investigate the efficacy, tolerability and safety of a new, highly potent statin, cerivastatin, in diabetic hyperlipidaemia. Methods: This was a multinational, multicentre, double-blind, randomized study in type 2 diabetic patients with hypercholesterolaemia (LDL cholesterol > 3.35 mmol/l; triglycerides <4.56 mmol/l). Eligible patients were randomly assigned to groups to receive cerivastatin 0.1 mg or 0.3 mg or placebo in a ratio of 2:2:1 for 12 weeks. They were monitored in the clinic every 4 weeks. Results: Of the 453 patients screened, 265 were allocated to the study groups. Fifty-one received placebo and 107 patients were assigned to each active treatment group (0.1 mg and 0.3 mg cerivastatin). At the close of the study, total cholesterol had decreased by 13.7% and 23.5%, LDL cholesterol decreased by 20.2% and 33.8%, and triglyceride concentrations decreased by 3.9% and 12.3% in the cerivastatin 0.1 mg and 0.3 mg groups, respectively. There was no significant difference between the groups in haemoglobin A(1c), adverse events or increases in liver and muscle enzymes during the study period. Conclusions: Hypercholesterolaemic patients with type 2 diabetes had a significant reduction in LDL cholesterol and total cholesterol concentrations after cerivastatin treatment once daily. The dose of 0.3 mg cerivastatin is effective in diabetic hypercholesterolaemia, with co-reduction of triglyceride concentrations. The effect of cerivastatin on coronary morbidity and mortality is currently being investigated in clinical trials.

CT Medical Descriptors:
*hypercholesterolemia: CO, complication
*hypercholesterolemia: DT, drug therapy
*non insulin dependent diabetes mellitus
drug efficacy
drug safety
dose response

drug tolerability
drug potency
cholesterol blood level
triacylglycerol blood level
protein blood level
enzyme blood level
flu like syndrome: ET, etiology
flu like syndrome: SI, side effect
upper respiratory tract infection: CO, complication
human
male
female
major clinical study
clinical trial
randomized controlled trial
double blind procedure
multicenter study
controlled study
aged
adult
article
priority journal
Drug Descriptors:
*cerivastatin: AE, adverse drug reaction
*cerivastatin: CT, clinical trial
*cerivastatin: CB, drug combination
*cerivastatin: DO, drug dose
*cerivastatin: IT, drug interaction
*cerivastatin: DT, drug therapy
*cerivastatin: PD, pharmacology
*cerivastatin: PO, oral drug administration
*hydroxymethylglutaryl coenzyme A reductase inhibitor: AE, adverse drug reaction
*hydroxymethylglutaryl coenzyme A reductase inhibitor: CT, clinical trial
*hydroxymethylglutaryl coenzyme A reductase inhibitor: CB, drug combination
*hydroxymethylglutaryl coenzyme A reductase inhibitor: DO, drug dose
*hydroxymethylglutaryl coenzyme A reductase inhibitor: IT, drug interaction
*hydroxymethylglutaryl coenzyme A reductase inhibitor: DT, drug therapy
*hydroxymethylglutaryl coenzyme A reductase inhibitor: PD, pharmacology
*hydroxymethylglutaryl coenzyme A reductase inhibitor: PO, oral drug administration
low density lipoprotein cholesterol: EC, endogenous compound
triacylglycerol: EC, endogenous compound
hemoglobin A1c: EC, endogenous compound
liver enzyme: EC, endogenous compound
muscle enzyme: EC, endogenous compound
nitrate: CB, drug combination
nitrate: IT, drug interaction
acetylsalicylic acid: CB, drug combination
acetylsalicylic acid: IT, drug interaction
beta adrenergic receptor blocking agent: CB, drug combination
beta adrenergic receptor blocking agent: IT, drug interaction
calcium channel blocking agent: CB, drug combination
calcium channel blocking agent: IT, drug interaction
dipeptidyl carboxypeptidase inhibitor: CB, drug combination
dipeptidyl carboxypeptidase inhibitor: IT, drug interaction
metformin: CB, drug combination
metformin: IT, drug interaction

glibenclamide: CB, drug combination
glibenclamide: IT, drug interaction
acarbose: CB, drug combination
acarbose: IT, drug interaction
RN (cerivastatin) 143201-11-0; (hemoglobin A1c) 62572-11-6; (nitrate) 14797-55-8; (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1; (metformin) 1115-70-4, 657-24-9; (glibenclamide) 10238-21-8; (acarbose) 56180-94-0
CN Aspirin

L62 ANSWER 35 OF 41 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 1999346115 EMBASE Full-text
TITLE: UKPDS: Implications for management of type 2 diabetes in the Millennium. The abiding legacy of Robert Turner.
AUTHOR: Campbell I.
SOURCE: Practical Diabetes International, (1999) Vol. 16, No. 6, pp. 161-162.
Refs: 0
ISSN: 1357-8170 CODEN: PDINFY
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
017 Public Health, Social Medicine and Epidemiology
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Oct 1999
Last Updated on STN: 21 Oct 1999
CT Medical Descriptors:
*non insulin dependent diabetes mellitus: DT, drug therapy
*non insulin dependent diabetes mellitus: DM, disease management
*blood glucose monitoring
*blood pressure regulation
United Kingdom
hypertension: DT, drug therapy
hypertension: PC, prevention
cardiovascular disease: DT, drug therapy
human
editorial
Drug Descriptors:
glucose: EC, endogenous compound
sulfonylurea: CB, drug combination
sulfonylurea: DT, drug therapy
insulin: DT, drug therapy
metformin: CB, drug combination
metformin: DT, drug therapy
captopril: DT, drug therapy
atenolol: DT, drug therapy
repaglinide: CB, drug combination
repaglinide: DT, drug therapy
rosiglitazone: CB, drug combination
rosiglitazone: DT, drug therapy
statin: DT, drug therapy
acetylsalicylic acid: DT, drug therapy
RN (glucose) 50-99-7, 84778-64-3; (insulin) 9004-10-8; (metformin) 1115-70-4, 657-24-9; (captopril) 62571-86-2; (atenolol) 29122-68-7; (repaglinide) 135062-02-1; (rosiglitazone) 122320-73-4; (acetylsalicylic

acid) 493-53-8, 50-78-2, 53663-74-4, 53664-49-6, 63781-77-1

L62 ANSWER 36 OF 41 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1998020371 EMBASE Full-text
TITLE: Management of dyslipidemia in adults with diabetes.
AUTHOR: Haffner S.M.
CORPORATE SOURCE: Dr. S.M. Haffner, Department of Medicine, Univ. of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284-7873, United States
SOURCE: Diabetes Care, (1998) Vol. 21, No. 1, pp. 160-178. .
Refs: 235
ISSN: 0149-5992 CODEN: DICAD2
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 5 Feb 1998
Last Updated on STN: 5 Feb 1998

AB Subjects with diabetes have a greatly increased risk of CHD, which is only partially related to their elevated glucose. Other factors such as insulin resistance and dyslipidemia are likely to be important. The type of dyslipidemia that is most characteristic of type 2 diabetic subjects is elevated triglycerides and decreased HDL cholesterol levels, although all lipoproteins have compositional abnormalities. Surprisingly few good prospective studies of lipoprotein levels in relation to CHD have been done in diabetic subjects. Available studies suggest that low HDL cholesterol may be the most important risk factor for CHD in observational studies. In studies in which total cholesterol and triglyceride were done, cholesterol and triglycerides were risk factors for CHD, although triglycerides were often a stronger predictor. However, the strength of triglyceride as a risk factor for CHD may depend partially on its association with other variables (e.g., hypertension, plasminogen activator inhibitor 1 [PAI-1], etc.). In clinical trials in diabetic subjects, LDL reduction with statins has led to significant reductions in CHD incidence. In addition, overall mortality was reduced with statin therapy, although the results were not statistically significant. Gemfibrozil has led to reductions in CHD incidence in diabetic subjects, although the results were not statistically significant perhaps because of low sample size. Regarding lipoproteins and CHD risk in diabetic patients, the very positive results of statin trials point to LDL cholesterol being more important than previously realized. Apparently, having a borderline high LDL cholesterol (between 130 and 160 mg/dl) in a diabetic patient is equivalent to a much higher LDL cholesterol in terms of CHD risk for a nondiabetic subject. Therefore, the primary target of therapy in diabetic patients is lowering LDL cholesterol (or possibly, non-HDL cholesterol). Statins are the preferred pharmacological agent in this situation. Once LDL cholesterol levels have been lowered, attention can be given to treatment of residual hypertriglyceridemia and low HDL. The goal here is weight reduction and increased exercise. However, for selected patients, combining a fibric acid (or low-dose nicotinic acid) with a statin also can be considered. Reduction of LDL levels should take priority over reduction of triglycerides in combined hyperlipidemia because of the proven safety of the statin class of drugs as well as greater reduction in CHD incidence.

CT Medical Descriptors:
*dyslipidemia: DM, disease management

*dyslipidemia: DT, drug therapy
*dyslipidemia: EP, epidemiology
*dyslipidemia: TH, therapy
*ischemic heart disease: CO, complication
*ischemic heart disease: EP, epidemiology
*non insulin dependent diabetes mellitus: DT, drug therapy
*non insulin dependent diabetes mellitus: EP, epidemiology
*non insulin dependent diabetes mellitus: TH, therapy
insulin dependent diabetes mellitus: DT, drug therapy
insulin dependent diabetes mellitus: EP, epidemiology
hyperglycemia
glucose homeostasis
atherosclerosis
insulin resistance
diet therapy
kinesiotherapy
cost effectiveness analysis
gastrointestinal symptom: SI, side effect
liver toxicity: SI, side effect
rhabdomyolysis: SI, side effect
drug mixture
human
male
female
major clinical study
clinical trial
randomized controlled trial
double blind procedure
multicenter study
controlled study
review
Drug Descriptors:
*lipid: EC, endogenous compound
*lipoprotein: EC, endogenous compound
*hydroxymethylglutaryl coenzyme a reductase inhibitor: CT, clinical trial
*hydroxymethylglutaryl coenzyme a reductase inhibitor: DO, drug dose
*hydroxymethylglutaryl coenzyme a reductase inhibitor: DT, drug therapy
*hydroxymethylglutaryl coenzyme a reductase inhibitor: PD, pharmacology
*antilipemic agent: CT, clinical trial
*antilipemic agent: DO, drug dose
*antilipemic agent: DT, drug therapy
*antilipemic agent: PD, pharmacology
*bile acid: AE, adverse drug reaction
*bile acid: DT, drug therapy
*bile acid: PD, pharmacology
*nicotinic acid: AE, adverse drug reaction
*nicotinic acid: DT, drug therapy
*nicotinic acid: PD, pharmacology
tolbutamide: CT, clinical trial
tolbutamide: DT, drug therapy
insulin: CT, clinical trial
insulin: DT, drug therapy
metformin: CT, clinical trial
metformin: DT, drug therapy
chlorpropamide: CT, clinical trial
chlorpropamide: DT, drug therapy
glibenclamide: CT, clinical trial
glibenclamide: DT, drug therapy
acarbose: CT, clinical trial
acarbose: DT, drug therapy

simvastatin: CT, clinical trial
simvastatin: CB, drug combination
simvastatin: DO, drug dose
simvastatin: DT, drug therapy
simvastatin: PR, pharmaceutics
simvastatin: PD, pharmacology
sulfonylurea derivative: CT, clinical trial
sulfonylurea derivative: DT, drug therapy
gemfibrozil: AE, adverse drug reaction
gemfibrozil: CB, drug combination
gemfibrozil: DO, drug dose
gemfibrozil: DT, drug therapy
gemfibrozil: EC, endogenous compound
gemfibrozil: PD, pharmacology
resin: AE, adverse drug reaction
resin: DO, drug dose
resin: DT, drug therapy
resin: EC, endogenous compound
resin: PD, pharmacology
pravastatin: CT, clinical trial
pravastatin: CB, drug combination
pravastatin: DO, drug dose
pravastatin: DT, drug therapy
pravastatin: EC, endogenous compound
pravastatin: PD, pharmacology
cholesterol: EC, endogenous compound
mevinolin: CT, clinical trial
mevinolin: CB, drug combination
mevinolin: DO, drug dose
mevinolin: DT, drug therapy
mevinolin: PD, pharmacology
fenofibrate: CT, clinical trial
fenofibrate: DO, drug dose
fenofibrate: DT, drug therapy
fenofibrate: PD, pharmacology
fibric acid derivative: CB, drug combination
fibric acid derivative: DO, drug dose
fibric acid derivative: DT, drug therapy
fibric acid derivative: PD, pharmacology
triacylglycerol
low density lipoprotein
high density lipoprotein
lipoprotein a

RN (lipid) 66455-18-3; (nicotinic acid) 54-86-4, 59-67-6; (tolbutamide) 473-41-6, 64-77-7; (insulin) 9004-10-8; (metformin) 1115-70-4, 657-24-9; (chlorpropamide) 94-20-2; (glibenclamide) 10238-21-8; (acarbose) 56180-94-0; (simvastatin) 79902-63-9; (gemfibrozil) 25812-30-0; (pravastatin) 81131-74-0; (cholesterol) 57-88-5; (mevinolin) 75330-75-5; (fenofibrate) 49562-28-9

L62 ANSWER 37 OF 41 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1998018054 EMBASE Full-text
TITLE: Lipid disorders in diabetes.
AUTHOR: Goldberg R.B.
CORPORATE SOURCE: Dr. R.B. Goldberg, Diabetes Research Institute (R77), Univ. of Miami School of Medicine, 1450 NW 10th Avenue, Miami, FL 33136, United States. rgoldbe1@mednet.med.miami.edu
SOURCE: Endocrinologist, (1997) Vol. 7, No. 6, pp. 436-442. .
Refs: 14

ISSN: 1051-2144 CODEN: EDOCEB
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 22 Jan 1998
Last Updated on STN: 22 Jan 1998

AB An increased frequency of lipid disorders is believed to be responsible, in part, for the increased prevalence of cardiovascular disease associated with diabetes. Decreased insulin action, attributable to insulin deficiency or insulin resistance, is the primary cause. Increased triglyceride and decreased high density lipoprotein (HDL) levels often associated with small, dense, low density lipoprotein (LDL) (dyslipidemia) are found more commonly than in nondiabetic patients, and elevated LDL values occur with equal frequency in overweight, elderly diabetic, and nondiabetic individuals. In addition, compositional abnormalities increase the atherogenicity of lipoproteins. These abnormalities are largely reversed by administration of high dosages of insulin in type 1 diabetic patients; in patients with type 2 diabetes, a dyslipidemic pattern frequently persists despite treatment with oral agents or insulin. Hypertriglyceridemia and low HDL are predictive of coronary heart disease (CHD) risk in diabetes, although hypertriglyceridemia loses its predictive power in patients with normal LDL levels or after correction for low HDL. Cut points for diagnosis and goals for treatment should be set lower for diabetic patients than for the general population. Weight reduction and increased physical activity are useful initial approaches to therapy. Recent evidence in diabetic patients with CHD that lowering LDL using statin drugs is associated with at least the same relative degree of benefit as in nondiabetic patients provides the rationale for aggressive LDL lowering in diabetic individuals, given their excess rate of CHD. Pharmacotherapy for hypertriglyceridemia is more controversial except in patients with severe abnormalities.

CT Medical Descriptors:
*dyslipidemia: DT, drug therapy
*dyslipidemia: TH, therapy
*insulin dependent diabetes mellitus: DT, drug therapy
*non insulin dependent diabetes mellitus: DT, drug therapy
weight reduction
physical activity
caloric restriction
ischemic heart disease
hypertriglyceridemia: DT, drug therapy
hypertriglyceridemia: TH, therapy
human
clinical trial
oral drug administration
review
Drug Descriptors:
*lipid: EC, endogenous compound
*antilipemic agent: DT, drug therapy
*hydroxymethylglutaryl coenzyme a reductase inhibitor: CT, clinical trial
*hydroxymethylglutaryl coenzyme a reductase inhibitor: DT, drug therapy
*insulin: DT, drug therapy
*oral antidiabetic agent: DT, drug therapy
*lipoprotein a: EC, endogenous compound
cholesterol: EC, endogenous compound
triacylglycerol: EC, endogenous compound

high density lipoprotein cholesterol: EC, endogenous compound
low density lipoprotein cholesterol: EC, endogenous compound
very low density lipoprotein: EC, endogenous compound
simvastatin: CT, clinical trial
simvastatin: DT, drug therapy
pravastatin: CT, clinical trial
pravastatin: DT, drug therapy
gemfibrozil: CT, clinical trial
gemfibrozil: DT, drug therapy
sulfonylurea derivative: DT, drug therapy
metformin: DT, drug therapy
troglitazone: DT, drug therapy
fluindostatin: DT, drug therapy
mevinolin: DT, drug therapy
atorvastatin: DT, drug therapy
nicotinic acid: DT, drug therapy
RN (lipid) 66455-18-3; (insulin) 9004-10-8; (cholesterol) 57-88-5; (simvastatin) 79902-63-9; (pravastatin) 81131-74-0; (gemfibrozil) 25812-30-0; (metformin) 1115-70-4, 657-24-9; (troglitazone) 97322-87-7; (fluindostatin) 93957-54-1; (mevinolin) 75330-75-5; (atorvastatin) 134523-00-5, 134523-03-8; (nicotinic acid) 54-86-4, 59-67-6

L62 ANSWER 38 OF 41 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2002-14642 DRUGU T Full-text
TITLE: Nephropathy in patients with type 2 diabetes.
AUTHOR: Remuzzi G; Schieppati A; Ruggenenti P
CORPORATE SOURCE: Inst.Res.Pharmacol.Mario-Negri
LOCATION: Bergamo, It.
SOURCE: N.Engl.J.Med. (346, No. 15, 1145-51, 2002) 1 Fig. 3 Tab. 43 Ref.
CODEN: NEJMAG ISSN: 0028-4793
AVAIL. OF DOC.: Mario Negri Institute, Via Gavazzeni 11, 24100 Bergamo, Italy. (A.S.).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Nephropathy in patients with type 2 diabetes is reviewed. Strategies and evidence supporting the use of microalbuminuria screening, glycemic control and B.P. control in managing diabetic nephropathy are discussed. The potential roles of metformin, ACE inhibitors (captopril, enalapril, lisinopril, ramipril and trandolapril), angiotensin II-receptor antagonists (losartan, valsartan and irbesartan), antihypertensive agents (nifedipine, amlodipine, diltiazem, verapamil, lisinopril and candesartan) and beta-blockers (carvedilol) are evaluated. The importance of B.P. goals, the treatment of dyslipidemia and protein restriction are considered. Multidrug treatment including diuretics (chlorthalidone, hydrochlorthalidone, furosemide and spironolactone) is evaluated. Clinical-practice guidelines are reviewed and recommendations proposed.
AN 2002-14642 DRUGU T Full-text
T Therapeutics
39 Kidney
58 Vasoactive
69 Reviews
CT DIABETES *TR; NEPHROPATHY *TR; CARBOHYDRATE-METAB.DISORDER *TR; PANCREOPATHY *TR; REVIEW *FT; CASES *FT; IN-VIVO *FT; PROPHYLAXIS *FT; CONCOMITANT-DISEASE *FT; NEPHROTROPIC *FT; HYPOTENSIVE *FT
[01] MAIN-TOPIC *FT; HYPOTENSIVES *FT; TR *FT
[02] METFORMIN *TR; CAPTOPRIL *TR; ENALAPRIL *TR; LISINOPRIL *TR;

RAMIPRIL *TR; TRANDOLAPRIL *TR; LOSARTAN *TR; VALSARTAN *TR; IRBESARTAN *TR; NIFEDIPINE *TR; AMLODIPINE *TR; DILTIAZEM *TR; VERAPAMIL *TR; CARVEDILOL *TR; CANDESARTAN *TR; CHLORTALIDONE *TR; HYDROCHLORTHALIDONE *TR; FUROSEMIDE *TR; SPIRONOLACTONE *TR; TR *FT

L62 ANSWER 39 OF 41 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-45400 DRUGU T Full-text
TITLE: Pharmacological treatment of obesity.
AUTHOR: Thissen J P
CORPORATE SOURCE: Univ.Louvain-Cath.
LOCATION: Louvain, Belg.
SOURCE: J.Pharm.Belg. (56, No. 2, 45-50, 2001) 4 Ref.
CODEN: JPBEAJ ISSN: 0047-2166
AVAIL. OF DOC.: Endocrinologie et Nutrition, Cliniques Universitaires St-Luc Universite Catholique de Louvain, Belgium.
LANGUAGE: French
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Pharmacological treatment of obesity is reviewed. Obesity may be complicated by syndrome X, symptoms of which include insulin resistance, arterial hypertension and abnormal triglyceride and cholesterol levels. Treatment involves weight loss and control of symptoms of syndrome X. Orlistat (OT) and sibutramine (SB) may be used to treat obesity; metformine, sulphonyl ureas, alpha-glucosidase inhibitors, insulin and thiazolidinediones may be used to treat type II diabetes; CEI, beta-blockers, calcium channel blockers and diuretics may be used in the treatment of arterial hypertension, and fibrates and statins may be used to treat abnormal triglyceride and cholesterol levels. (conference paper: Conference on Pathology and Nutrition, Louvain, Belgium, 2000).
AN 2001-45400 DRUGU T Full-text
T Therapeutics
58 Vasoactive
69 Reviews
CT OBESITY *TR; BODY-WEIGHT *TR; CASES *FT; IN-VIVO *FT; REVIEW *FT; ANORECTIC *FT
[01] MAIN-TOPIC *FT; ANORECTICS *FT; TR *FT
[02] ORLISTAT *TR; SIBUTRAMINE *TR; METFORMIN *TR; ACARBOSE *TR; TROGLITAZONE *TR; CAPTOPRIL *TR; TR *FT

L62 ANSWER 40 OF 41 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2000-36337 DRUGU T B E Full-text
TITLE: Are postprandial triglyceride and insulin abnormalities neglected cardiovascular risk factors in type 2 diabetes
AUTHOR: Golay A
CORPORATE SOURCE: Univ.Geneva
LOCATION: Geneva, Switz.
SOURCE: Eur.J.Clin.Invest. (30, Suppl. 2, 12-18, 2000) 3 Fig. 1 Tab. 54 Ref.
CODEN: EJCIB8 ISSN: 0014-2972
AVAIL. OF DOC.: Division d'Enseignement, Therapeutic pour Maladies Chroniques (3HL), Geneva University Hospital, 24, rue Micheli du Crest, 1211 Geneva 14, Switzerland. (e- mail: alain.golay@hcuge.ch).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Postprandial triglyceride and insulin abnormalities as neglected cardiovascular risk factors in type 2 diabetes are reviewed. Postprandial

metabolism in nondiabetic and type 2 diabetic patients are mentioned. Insulin resistance and lipid profiles are cited. Management of postprandial hyperinsulinemia (miglitol, acarbose, metformin and sulphonylureas) and hypertriglyceridemia (ciprofibrate, fenofibrate and statins) is discussed. Lifestyle modifications and appropriate choice of glucose- and lipid-lowering drugs are targeted to treat the pattern of lipid abnormalities associated with type 2 diabetes. (conference paper: Satellite Symposium held at the 35th Annual Meeting of the European Association for the Study of Diabetes, Brussels, Belgium, 1999).

AN 2000-36337 DRUGU T B E Full-text
T Therapeutics
B Biochemistry
E Endocrinology
12 Antidiabetics
22 Endogenous Compounds
58 Vasoactive
69 Reviews

CT DIABETES *TR; HYPERINSULINISM *TR; HYPERTRIGLYCERIDEMIA *TR; CARDIOPATHY *TR; VASCULAR-DISEASE *TR; CARBOHYDRATE-METAB.DISORDER *TR; PANCREOPATHY *TR; CARBOHYDRATE-METAB.DISORDER *TR; PANCREOPATHY *TR; LIPID-METAB.DISORDER *TR; IN-VIVO *FT; CASES *FT; REVIEW *FT; POSTPRANDIAL *FT; TRIGLYCERIDE *FT; LIPID-METAB. *FT
[01] MIGLITOL *TR; ACARBOSE *TR; METFORMIN *TR; CIPROFIBRATE *TR; FENOFIBRATE *TR; MAIN-TOPIC *FT; TR *FT

L62 ANSWER 41 OF 41 DRUGU COPYRIGHT 2007 THE THOMSON CORP on STN
ACCESSION NUMBER: 2001-02646 DRUGU T S E Full-text
TITLE: Pioglitazone in the treatment of type 2 diabetes mellitus: U.S. clinical experience.
AUTHOR: Buse J B
LOCATION: Chapel Hill, N.C., USA
SOURCE: Exp.Clin.Endocrinol.Diabetes (108, Suppl. 2, S250-S255, 2000)
1 Fig. 3 Tab. 22 Ref.
CODEN: ECEDF ISSN: 0947-7349
AVAIL. OF DOC.: University of North Carolina School of Medicine, Diabetes Care Center, 5316 Highgate Drive, Durham, NC 27713, U.S.A.
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

AB Pioglitazone was employed as monotherapy and in a variety of combination therapy regimens in adult patients with type 2 diabetes in a meta-analysis of 6 randomized, placebo-controlled, multicenter, parallel-group, double-blind, pivotal trials in the United States. Pioglitazone reduced glucose AUC in a dose-related fashion following a p.o. glucose challenge. Pioglitazone reduced serum triglycerides and raised HDL-cholesterol levels without causing any consistent mean change from placebo in total or LDL-cholesterol. Edema, weight gain, and decreased Hb/hematocrit were seen more commonly with pioglitazone compared with placebo. Data show that the preponderance of combination therapy in U.S. clinical practice may reveal a tendency among some physicians to reserve pioglitazone for patients who have failed therapy with more familiar agents such as sulphonylureas or metformin.

AN 2001-02646 DRUGU T S E Full-text
T Therapeutics
S Adverse Effects
E Endocrinology
12 Antidiabetics
35 Adverse Reactions
64 Clinical Trials
69 Reviews

CT DIABETES *TR; CARBOHYDRATE-METAB.DISORDER *TR; PANCREOPATHY *TR; CASES *FT; IN-VIVO *FT; REVIEW *FT; CLIN.TRIAL *FT

[01] PIOGLITAZONE *TR; PIOGLITAZONE *AE; AD-4833 *RN; MAIN-TOPIC *FT; ANTIDIABETIC *FT; ANTIDIABETICS *FT; ANTIARTERIOSCLEROTICS *FT; TR *FT; AE *FT

[02] ROSIGLITAZONE *AE; TROGLITAZONE *AE; AE *FT

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=> d his nofile

     (FILE 'HOME' ENTERED AT 09:24:40 ON 19 JUL 2007)

     FILE 'HCAPLUS' ENTERED AT 09:24:48 ON 19 JUL 2007
L1             1 SEA ABB=ON  PLU=ON  US20060240095/PN
                 SEL RN

     FILE 'REGISTRY' ENTERED AT 09:26:12 ON 19 JUL 2007
L2             9 SEA ABB=ON  PLU=ON  (657-24-9/BI OR 134523-00-5/BI OR 147511-69
                 -1/BI OR 287714-41-4/BI OR 75330-75-5/BI OR 79902-63-9/BI OR
                 81093-37-0/BI OR 9028-35-7/BI OR 93957-54-1/BI)
L3             1 SEA ABB=ON  PLU=ON  9028-35-7/RN

     FILE 'HCAPLUS' ENTERED AT 09:28:02 ON 19 JUL 2007
L4          9118 SEA ABB=ON  PLU=ON  L3

     FILE 'REGISTRY' ENTERED AT 09:28:53 ON 19 JUL 2007
L5             2 SEA ABB=ON  PLU=ON  STATIN/CN

     FILE 'HCAPLUS' ENTERED AT 09:30:24 ON 19 JUL 2007
L6          7933 SEA ABB=ON  PLU=ON  L5

     FILE 'HCAPLUS' ENTERED AT 09:30:57 ON 19 JUL 2007
L7          2862 SEA ABB=ON  PLU=ON  METFORMIN/OBI
L8          2633 SEA ABB=ON  PLU=ON  657-24-9/RN
L9            48 SEA ABB=ON  PLU=ON  657-24-9D/RN
L10         3100 SEA ABB=ON  PLU=ON  (L7 OR L8 OR L9)
L11          191 SEA ABB=ON  PLU=ON  L10 AND L5
L12         4745 SEA ABB=ON  PLU=ON  STATIN/OBI
L13        11420 SEA ABB=ON  PLU=ON  L12 OR L5
L14          218 SEA ABB=ON  PLU=ON  L13 AND L10

     FILE 'ZCAPLUS' ENTERED AT 09:34:47 ON 19 JUL 2007
L15              QUE ABB=ON  PLU=ON  STATIN
L16              QUE ABB=ON  PLU=ON  METFORMIN
L17              QUE ABB=ON  PLU=ON  HYPERGLYCEMI? OR DIABETE# METILLUS
L18              QUE ABB=ON  PLU=ON  HYPERGLYCEMI? (2A) AGENT#
L19              QUE ABB=ON  PLU=ON  DIABET? (2A) (TYPE 2 OR TYPE II OR TYPE
                 TWO)
L20              QUE ABB=ON  PLU=ON  JUNIEN J?/AU
L21              QUE ABB=ON  PLU=ON  JUNIEN JEAN LOUIS/AU
L22              QUE ABB=ON  PLU=ON  EDGAR A?/AU
L23              QUE ABB=ON  PLU=ON  AY<2003 OR PY<2003 OR PRY<2003
L24              QUE ABB=ON  PLU=ON  AY<2003 OR PY<2003 OR PRY<2003 OR MY<2003
                 OR REVIEW/DT

     FILE 'HCAPLUS' ENTERED AT 09:37:40 ON 19 JUL 2007
L25           53 SEA ABB=ON  PLU=ON  (L11 OR L14) AND ((L17 OR L18 OR L19))
L26           22 SEA ABB=ON  PLU=ON  L25 AND L24
L27            0 SEA ABB=ON  PLU=ON  L26 AND L1
L28            1 SEA ABB=ON  PLU=ON  L25 AND L1
L29            5 SEA ABB=ON  PLU=ON  L26 (P) (COMBINATION#/OBI OR DOSAGE#/OBI
                 OR DOSING/OBI OR ADMINISTER?/OBI)

     FILE 'STNGUIDE' ENTERED AT 09:43:09 ON 19 JUL 2007

     FILE 'HCAPLUS' ENTERED AT 09:44:39 ON 19 JUL 2007
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                SAVE TEMP L29 KUD523HCAP/A
L30          187 SEA ABB=ON  PLU=ON  JUNIEN J?/AU
L31           95 SEA ABB=ON  PLU=ON  JUNIEN JEAN LOUIS/AU
L32          295 SEA ABB=ON  PLU=ON  EDGAR A?/AU
L33            6 SEA ABB=ON  PLU=ON  L32 AND ((L30 OR L31))
L34            5 SEA ABB=ON  PLU=ON  L33 NOT L1
                 SAVE TEMP L34 KUD523HCAPIN/A

     FILE 'STNGUIDE' ENTERED AT 09:47:18 ON 19 JUL 2007

     FILE 'WPIX' ENTERED AT 09:51:45 ON 19 JUL 2007
L35           45 SEA ABB=ON  PLU=ON  L15 AND L16
L36         6049 SEA ABB=ON  PLU=ON  (L17 OR L18 OR L19)
L37           22 SEA ABB=ON  PLU=ON  L35 AND L36
L38            1 SEA ABB=ON  PLU=ON  L37 AND L1
L39            1 SEA ABB=ON  PLU=ON  L37 AND L33
L40            9 SEA ABB=ON  PLU=ON  L37 AND L23
                 SAVE TEMP L40 KUD523WPIX/A
L41           35 SEA ABB=ON  PLU=ON  (L30 OR L31)
L42          105 SEA ABB=ON  PLU=ON  EDGAR A?/AU
L43            7 SEA ABB=ON  PLU=ON  L41 AND L42
L44            7 SEA ABB=ON  PLU=ON  L43 NOT L40
L45            6 SEA ABB=ON  PLU=ON  L43 NOT L1
                 SAVE TEMP L45 KUD523WPIXIN/A

     FILE 'MEDLINE, BIOSIS, EMBASE, DRUGU, BIOTECHNO, PASCAL, CONFSCI' ENTERED
     AT 09:56:47 ON 19 JUL 2007
L46          443 SEA ABB=ON  PLU=ON  L35
L47       238391 SEA ABB=ON  PLU=ON  L36
L48          265 SEA ABB=ON  PLU=ON  L46 AND L47
L49           74 SEA ABB=ON  PLU=ON  L48 AND L24
L50           29 SEA ABB=ON  PLU=ON  L49 AND (COMBINATION# OR DOSAGE# OR DOSING
                 OR ADMINISTER?)
L51           29 SEA ABB=ON  PLU=ON  L49 (P) (COMBINATION# OR DOSAGE# OR DOSING
                 OR ADMINISTER?)
L52            1 SEA ABB=ON  PLU=ON  L49 AND (CAPSULE# OR DRAGEE# OR GRANULE#
                 OR POWDER# OR SACHET# OR TABLET# OR SUSPENSION#)
L53           29 SEA ABB=ON  PLU=ON  L51 OR L52
                 SAVE TEMP L53 KUD523MULTI/A
L54            0 SEA ABB=ON  PLU=ON  L41 AND L32
L55          719 SEA ABB=ON  PLU=ON  L41
L56          474 SEA ABB=ON  PLU=ON  L32
L57           12 SEA ABB=ON  PLU=ON  L55 AND ((L35 OR L36))
L58            5 SEA ABB=ON  PLU=ON  L56 AND ((L35 OR L36))
L59           17 SEA ABB=ON  PLU=ON  L57 OR L58
L60           17 SEA ABB=ON  PLU=ON  L59 AND L24
                 SAVE L60 TEMP KUD523MULTIN/A

     FILE 'STNGUIDE' ENTERED AT 10:25:38 ON 19 JUL 2007
                 D QUE L34
                 D QUE L45
                 D QUE L60

     FILE 'HCAPLUS, WPIX, MEDLINE, BIOSIS, EMBASE, DRUGU, BIOTECHNO, PASCAL'
     ENTERED AT 10:29:00 ON 19 JUL 2007
L61           12 DUP REM L34 L45 L60 (16 DUPLICATES REMOVED)
                      ANSWERS '1-5' FROM FILE HCAPLUS
                      ANSWER '6' FROM FILE WPIX
                      ANSWERS '7-9' FROM FILE MEDLINE
                      ANSWERS '10-12' FROM FILE BIOSIS
```

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                D 1-12 IBIB AB 1-12
                D QUE L29
                D QUE L40
                D QUE L53
L62          41 DUP REM L29 L40 L53 (2 DUPLICATES REMOVED)
                     ANSWERS '1-5' FROM FILE HCAPLUS
                     ANSWERS '6-14' FROM FILE WPIX
                     ANSWERS '15-26' FROM FILE MEDLINE
                     ANSWERS '27-37' FROM FILE EMBASE
                     ANSWERS '38-41' FROM FILE DRUGU
                D L62 1-5 IBIB ED ABS HITIND
                D L62 6-14 IALL ABEQ TECH ABEX
                D L62 15-41 IBIB AB IND
```